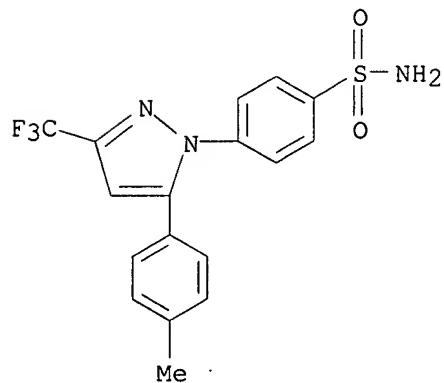


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=> s celecoxib/cn
L1          1 CELECOXIB/CN
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=> d
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L1      ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN      169590-42-5  REGISTRY
CN      Benzenesulfonamide,
4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-
yl]-(9CI)  (CA INDEX NAME)
OTHER NAMES:
CN      4-[5-(4-Methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-
yl]benzenesulfonamide
CN      Celebrex
CN      Celecoxib
CN      Celocoxib
CN      SC 58635
CN      YM 177
FS      3D CONCORD
DR      184007-95-2, 194044-54-7
MF      C17 H14 F3 N3 O2 S
CI      COM
SR      US Adopted Names Council
LC      STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS,
       BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN,
       CHEMCATS,
       CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES,
       EMBASE, IPA, MEDLINE, MRCK*, PHAR, PHARMASEARCH, PROMT, RTECS*,
       SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
       (*File contains numerically searchable property data)
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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

374 REFERENCES IN FILE CA (1967 TO DATE)
10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
379 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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=> s ethinyl estradiol/cn
L2          0 ETHINYL ESTRADIOL/CN
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=> fil uspatfull embase caplus medline biosis
 COST IN U.S. DOLLARS SINCE FILE TOTAL
 ENTRY SESSION
 FULL ESTIMATED COST 10.72 10.93

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FILE 'BIOSIS' ENTERED AT 14:30:14 ON 10 SEP 2002
 COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC. (R)

=> s 169590-42-5/rn
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 'RN' IS NOT A VALID FIELD CODE
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 L3 462 169590-42-5/RN

=> s 57-63-6/rn
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 'RN' IS NOT A VALID FIELD CODE
 L4 3885 57-63-6/RN

=> s 13 and 14
 L5 9 L3 AND L4

=> s 15 and dysmenorrhea
 L6 1 L5 AND DYSMENORRHEA

=> d 16

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
 AN 2002:615443 CAPLUS
 DN 137:150281
 TI Method of using a cyclooxygenase-2 inhibitor and sex steroids as a
 combination therapy for the treatment and prevention of
 dysmenorrhea
 IN Krasnow, Joel
 PA Pharmacia Corporation, USA
 SO PCT Int. Appl., 101 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1
 PATENT NO. KIND DATE APPLICATION NO. DATE
 PI WO 2002062391 A2 20020815 WO 2002-US203132 20020204
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
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 TJ, TM
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 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 PRAI US 2001-266261P P 20010202

=> dup rem 15
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 L7 8 DUP REM L5 (1 DUPLICATE REMOVED)

=> s 17 and py<2001
 3 FILES SEARCHED...
 L8 1 L7 AND PY<2001

=> d 18

L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
 AN 2000:861473 CAPLUS
 DN 134:32972
 TI Porous drug matrixes containing polymers and sugars and methods of their
 manufacture
 IN Straub, Julie; Bernstein, Howard; Chickering, Donald E., III; Khatak,
 Sarwat; Randall, Greg
 PA Acusphere, Inc., USA
 SO PCT Int. Appl., 45 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000072827	A2	20001207	WO 2000-US14578	20000525 <--
	WO 2000072827	A3	20010125		
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	EP 1180020	A2	20020220	EP 2000-939365	20000525
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	NO 2001005753	A	20020128	NO 2001-5753	20011126
PRAI	US 1999-136323P	P	19990527		
	US 1999-158659P	P	19991008		
	US 1999-433486	A	19991104		
	US 2000-186310P	P	20000302		
	WO 2000-US14578	W	20000525		

=> d kwic

L8	ANSWER 1 OF 1	CAPLUS	COPYRIGHT 2002 ACS		
PI	WO 2000072827	A2	20001207		
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000072827	A2	20001207	WO 2000-US14578	20000525 <--
	WO 2000072827	A3	20010125		
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IT	50-28-2, Estradiol, biological studies	50-35-1, Thalidomide	50-99-7, Dextrose, biological studies	52-53-9, Verapamil	53-03-2, Prednisone
	55-98-1, Busulfan	57-63-6, Ethinyl estradiol	58-61-7, Adenosine, biological studies	59-92-7, Levodopa, biological studies	67-78-7 67-97-0, Vitamin D3
	67-97-0D, Vitamin D3, analogs	71-58-9, Medroxyprogesterone acetate	75-64-9, Erbumine, biological studies	75-64-9, Carbamazepine	77-36-1, Chlorthalidone
	89-57-6, Mesalamine	126-07-8, Griseofulvin	126-07-8, Tretinoin	298-46-4, Ursodiol	128-13-2, Tacrine
	302-79-4, Fentanyl	321-64-2, Dinoprostone	437-38-7, Diazepam	363-24-6, Metronidazole	439-14-5, Alaprostadil
	518-28-5, Podofilox	443-48-1, Lorazepam	518-28-5, Amiodarone	484-49-1, Isotretinoin	745-65-3, Dexfenfluramine
	5534-09-8, Beclomethasone dipropionate	4759-48-2, Betamethasone dipropionate	5534-09-8, Growth hormone	5593-20-4, Follitropin	67-97-0, Vitamin D3
	9002-68-0, Calcitonin	9002-72-6, Enoxaparin	9005-49-6, Enoxaparin, biological studies	9002-72-6, Alprostadil	71-58-9, Adenosine, biological studies
	9041-93-4, Glyburide	100238-21-8, Chlorthalidone	100238-21-8, Carbamazepine	10238-21-8, Ursodiol	75-64-9, Ethinyl estradiol
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	12629-01-5, Amphotericin	12633-72-6, Albuterol	12629-01-5, Griseofulvin	363-24-6, Dinoprostone	89-57-6, Verapamil
	13311-84-7, Flutamide	20830-75-5, Digoxin	13311-84-7, Fentanyl	437-38-7, Metronidazole	128-13-2, Ursodiol
	15307-79-6, Diclofenac	21256-18-8, Fentanyl	15307-86-5, Diazepam	518-28-5, Podofilox	128-13-2, Tacrine
	15687-27-1, Ibuprofen	22204-53-1, Alprazolam	518-28-5, Amiodarone	443-48-1, Lorazepam	439-14-5, Alaprostadil
	18559-94-9, Albuterol	27203-92-5, Naproxen	5534-09-8, Dexfenfluramine	484-49-1, Isotretinoin	745-65-3, Dexfenfluramine
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	40391-99-9, 41340-25-4, Etodolac	42399-41-7, Diltiazem	5593-20-4, Growth hormone	9002-72-6, Ursodiol	128-13-2, Diclofenac sodium
	41575-94-4, Carboplatin	42399-41-7, Diltiazem	5593-20-4, Enoxaparin	9002-72-6, Somatropin	128-13-2, Ursodiol
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	69655-05-6, Didanosine	70476-82-3, Mitoxantrone hydrochloride	72432-03-2, Miglitol	9002-72-6, Ursodiol	128-13-2, Ursodiol

72509-76-3, Felodipine 72558-82-8, Ceftazidime 72956-09-3, Carvedilol
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 Nizatidine 77883-43-3, Doxazosin mesylate 78246-49-8, Paroxetine
 hydrochloride 78628-80-5, Terbinafine hydrochloride 78755-81-4,
 Flumazenil 79517-01-4, Octreotide acetate 79559-97-0, Sertraline
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 80274-67-5, Metoprolol fumarate 81098-60-4, Cisapride 81103-11-9,
 Clarithromycin 82410-32-0, Ganciclovir 82752-99-6, Nefazodone
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 83905-01-5, Azithromycin 83919-23-7, Mometasone furoate 84625-61-6,
 Itraconazole 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole
 86541-74-4, Benazepril hydrochloride 86541-75-5, Benazepril
 87679-37-6, Trandolapril 89778-27-8, Toremifene citrate 91161-71-6,
 Terbinafine 91421-42-0, Rubitecan 93413-69-5, Venlafaxine
 93957-54-1, Fluvastatin 95058-81-4, Gemcitabine 95233-18-4,
Atovaquone
 97048-13-0, Urofollitropin 97322-87-7, Troglitazone 98048-97-6,
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 Finasteride 99011-02-6, Imiquimod 99294-93-6, Zolpidem tartrate
 100286-90-6, Irinotecan hydrochloride 100986-85-4, Levofloxacin
 103577-45-3, Lansoprazole 103628-48-4, Sumatriptan succinate
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 Tamsulosin hydrochloride 106685-40-9, Adapalene 107753-78-6,
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 111470-99-6, Amlodipine besylate 111974-72-2, Quetiapine fumarate
 112809-51-5, Letrozole 113806-05-6, Olopatadine 114798-26-4, Losartan
 114977-28-5, Docetaxel 115956-12-2, Dolasetron 120014-06-4, Donepezil
 124832-26-4, Valacyclovir 127779-20-8, Saquinavir 131918-61-1,
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 143011-72-7, Granulocyte colony-stimulating factor 144701-48-4,
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 159989-65-8, Nelfinavir mesylate 161814-49-9, Amprenavir 162011-90-7,
 Rofecoxib 169590-42-5, Celecoxib 171599-83-0, Sildenafil
 citrate
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
 use); BIOL (Biological study); PROC (Process); USES (Uses)
 (prepn. of porous matrixes contg. hydrophilic polymers and sugars for
 enhancement of drug dissoln.)

=> d ab

L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
 AB Drugs, esp. low aq. solv. drugs, are provided in a porous matrix form,
 preferably microparticles, which enhances dissoln. of the drug in aq.
 media. The drug matrixes preferably are made using a process that
 includes (i) dissolving a drug, preferably a drug having low aq. solv.,
 in
 a volatile solvent to form a drug soln., (ii) combining at least one pore
 forming agent with the drug soln. to form an emulsion, suspension, or
 second solns., and (iii) removing the volatile solvent and pore forming
 agent from the emulsion, suspension, or second soln. to yield the porous

matrix of drug. The pore forming agent can be either a volatile liq. that is immiscible with the drug solvent or a volatile solid compd., preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aq. medium and administered parenterally, or processed using std. techniques into tablets or capsules for oral administration. Paclitaxel or docetaxel can be provided in a porous matrix form, which allows the drug to be formulated without solubilizing agents and administered as a bolus. For example, a nifedipine-loaded org. soln. was prep'd. by dissolving 9.09 g of PEG 3350, 2.27 g of nifedipine, and 0.009 g of lecithin in 182 mL of methylene chloride. An aq. soln. was prep'd. by dissolving 3.27 g of NH4HCO3 and 0.91 g of PEG 3350 in 1.82 mL of water. The aq. and org. solns. were homogenized and resulting emulsion was spray dried. A suspension of the porous nifedipine drug matrix was prep'd. in 5% dextrose soln. at a concn. of 2.5 mg/mL. A bolus injection of the suspension was tolerated when administrated to dogs.

=> d hist
(FILE 'HOME' ENTERED AT 14:28:23 ON 10 SEP 2002)
FILE 'REGISTRY' ENTERED AT 14:28:30 ON 10 SEP 2002
L1 1 S CELECOXIB/CN
L2 0 S ETHINYLN ESTRADIOL/CN
FILE 'USPATFULL, EMBASE, CAPLUS, MEDLINE, BIOSIS' ENTERED AT 14:30:14 ON 10 SEP 2002
L3 462 S 169590-42-5/RN
L4 3885 S 57-63-6/RN
L5 9 S L3 AND L4
L6 1 S L5 AND DYSMENORRHEA
L7 8 DUP REM L5 (1 DUPLICATE REMOVED)
L8 1 S L7 AND PY<2001
=> s l1 and dysmenorrhea
L9 49 L1 AND DYSMENORRHEA
=> dup rem 19
PROCESSING COMPLETED FOR L9
L10 46 DUP REM L9 (3 DUPLICATES REMOVED)
=> s l10 and py<2001
3 FILES SEARCHED...
L11 11 L10 AND PY<2001
=> d l11 1-11 ab bib kwic
L11 ANSWER 1 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AB A new class of analgesics is expanding treatment options for osteoarthritis and rheumatoid arthritis.
AN 2002190778 EMBASE

TI Coxibs: Are they a potential alternative to NSAIDs?.
AU Weatherston C.
CS C. Weatherston, Health Sciences Centre, Pharmacy Department, Winnipeg, Man., Canada
SO Canadian Pharmaceutical Journal, (2000) 133/3 (30-32).
Refs: 18
ISSN: 0828-6914 CODEN: CPJOAC
CY Canada
DT Journal; (Short Survey)
FS 031 Arthritis and Rheumatism
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
SO Canadian Pharmaceutical Journal, (2000) 133/3 (30-32).
Refs: 18
ISSN: 0828-6914 CODEN: CPJOAC
CT Medical Descriptors:
*osteoarthritis: DT, drug therapy
*rheumatoid arthritis: DT, drug therapy
*dysmenorrhea: DT, drug therapy
drug indication
drug induced disease: SI, side effect
gastrointestinal symptom: SI, side effect
drug cost
analgesia
kidney disease: SI, side effect
drug nomenclature
drug effect
human
short. . .
RN (celecoxib) 169590-42-5; (rofecoxib) 162011-90-7, 186912-82-3;
(naproxen) 22204-53-1, 26159-34-2; (warfarin) 129-06-6, 2610-86-8,
3324-63-8, 5543-58-8, 81-81-2

L11 ANSWER 2 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2001175358 EMBASE
TI Selective cyclooxygenase-2 inhibition: Biological and clinical effects.
AU Conti F.; Spinelli F.R.; Ossandon A.; Valesini G.
CS Dr. G. Valesini, Cattedra di Reumatologia, Univ. degli Studi Roma La Sapienza, Policlinico Umberto I, 00161 Rome, Italy. valesini@uniromal.it
SO Israel Medical Association Journal, (2000) 2/11 (841-847).
Refs: 45
ISSN: 1565-1088 CODEN: IMAJCX
CY Israel
DT Journal; General Review
FS 037 Drug Literature Index
030 Pharmacology
029 Clinical Biochemistry
038 Adverse Reactions Titles
031 Arthritis and Rheumatism
LA English
SO Israel Medical Association Journal, (2000) 2/11 (841-847).
Refs: 45
ISSN: 1565-1088 CODEN: IMAJCX
CT Medical Descriptors:
human
clinical . . . SI, side effect
drug absorption

drug blood level
antiinflammatory activity
kidney disease: SI, side effect
enzyme inhibition
kidney function
drug selectivity
prostaglandin synthesis inhibition
enzyme activity
bronchospasm: SI, side effect
IC 50
 dysmenorrhea: DT, drug therapy
nausea: SI, side effect
leg edema: SI, side effect
review
 *cyclooxygenase 2 inhibitor: PD, pharmacology
 *cyclooxygenase 2 inhibitor: AE, adverse drug.
RN. . . (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6,
63781-77-1; (rofecoxib) 162011-90-7, 186912-82-3; (ibuprofen) 15687-27-1;
(diclofenac) 15307-79-6, 15307-86-5; (methotrexate) 15475-56-6, 59-05-2,
7413-34-5; (celecoxib) **169590-42-5**; (5 (4 fluorophenyl) 1 [(4
methylsulfonyl)phenyl] 3 trifluoromethylpyrazole) 162054-19-5; (naproxen)
22204-53-1, 26159-34-2; (indometacin) 53-86-1, 74252-25-8, 7681-54-1;
(indobufen) 36690-96-7, 63610-08-2; (ketoprofen). . .

L11 ANSWER 3 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AB Cyclooxygenase-2 (COX-2) inhibitors constitute a new group of
non-steroidal anti-inflammatory drugs (NSAIDs) which, at recommended
doses, block prostaglandin production by cyclooxygenase-2, but not by
cyclooxygenase-1. Two COX-2 inhibitors are currently available in
Australia - celecoxib, which is taken twice daily, and rofecoxib, which
is taken once daily. Both drugs act rapidly in providing pain relief and
their anti-inflammatory analgesic effect in osteoarthritis and rheumatoid
arthritis is equivalent to standard doses of non-selective NSAIDs.
Celecoxib and rofecoxib show significantly lower incidences of
gastrotoxicity (as measured by endoscopic studies and gastrointestinal
ulcers and bleeds) than non-selective NSAIDs. There is Level 2 evidence
that COX-2 inhibitors: reduce pain in classic pain models - third-molar
extraction, dysmenorrhoea and after orthopaedic surgery; reduce pain and
disability in osteoarthritis of the hip and knee; and reduce pain and
disability in rheumatoid arthritis. Other adverse effects, such as
interference with antihypertensive agents and the potential to produce
renal dysfunction in patients with compromised renal function by COX-2
inhibitors, seem similar to those of non-selective NSAIDs.

AN 2000374230 EMBASE
TI Cox-2 inhibitors.
AU Brooks P.M.; Day R.O.
CS Prof. P.M. Brooks, Faculty of Health Sciences, University of Queensland,
Edith Cavell Building, Herston, QLD 4029, Australia
SO Medical Journal of Australia, (16 Oct 2000) 173/8 (433-436).
Refs: 25
ISSN: 0025-729X CODEN: MJAUAJ
CY Australia
DT Journal; Article
FS 030 Pharmacology
031 Arthritis and Rheumatism
033 Orthopedic Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LA English

SL English
SO Medical Journal of Australia, (16 Oct 2000) 173/8 (433-436).
Refs: 25
ISSN: 0025-729X CODEN: MJAUAJ

CT Medical Descriptors:
*musculoskeletal . . . arthritis: DT, drug therapy
*knee osteoarthritis: DT, drug therapy
analgesia
gastrointestinal symptom: SI, side effect
endoscopy
digestive system ulcer: SI, side effect
gastrointestinal hemorrhage: SI, side effect
 dysmenorrhea: DT, drug therapy
postoperative pain
kidney function
drug efficacy
nephrotoxicity: SI, side effect
cardiovascular disease: SI, side effect
infertility: SI, side effect
human
article
*cyclooxygenase 2 inhibitor: AE, . . .

RN (celecoxib) 169590-42-5; (rofecoxib) 162011-90-7, 186912-82-3;
(warfarin) 129-06-6, 2610-86-8, 3324-63-8, 5543-58-8, 81-81-2;
(methotrexate) 15475-56-6, 59-05-2, 7413-34-5; (lithium) 7439-93-2;
(furosemide) 54-31-9; (codeine) 76-57-3; (oxycodone). . .

L11 ANSWER 4 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AB Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit prostaglandin synthesis via the cyclooxygenase (COX) enzyme, the key to both therapeutic benefits and toxicity. COX enzyme exists in 2 isoforms, COX-1 and COX-2. COX-1 enzyme is thought to mediate 'housekeeping' or homeostatic functions, and COX-2 is considered an inducible enzyme in response to injury or inflammation. COX-2 inhibitors are the 'next-generation' NSAIDs that may selectively block the COX-2 isoenzyme without affecting COX-1 function. This may result in control of pain and inflammation with a lower rate of adverse effects compared with older nonselective NSAIDs. Rapidly evolving evidence suggests that COX-2 enzyme has a diverse physiologic and pathologic role. This article addresses the role of COX-2 enzyme in health and disease as well as the potential therapeutic value and safety issues related to COX-2 inhibition.

AN 2000348523 EMBASE
TI The 'aspirin' of the new millennium: Cyclooxygenase-2 inhibitors.
AU Buttar N.S.; Wang K.K.
CS Dr. K.K. Wang, Div. of Gastroenterology/Hepatology, Mayo Clinic, 200 First St. SW, Rochester, MN 55905, United States. wang.kenneth@mayo.edu
SO Mayo Clinic Proceedings, (2000) 75/10 (1027-1038).
Refs: 112
ISSN: 0025-6196 CODEN: MACPAJ
CY United States
DT Journal; General Review
FS 008 Neurology and Neurosurgery
011 Otorhinolaryngology
031 Arthritis and Rheumatism
037 Drug Literature Index

038 Adverse Reactions Titles

LA English

SL English

SO Mayo Clinic Proceedings, (2000) 75/10 (1027-1038).
Refs: 112
ISSN: 0025-6196 CODEN: MACPAJ

CT Medical Descriptors:
*pain: DT, drug therapy
*inflammation: DT, drug therapy
pain assessment
analgesia
homeostasis
drug safety
drug efficacy
rheumatoid arthritis: DT, drug therapy
osteoarthritis: DT, drug therapy
fever: DT, drug therapy
dysmenorrhea: DT, drug therapy
petechia: SI, side effect
gastroduodenal ulcer: SI, side effect
erosion: SI, side effect
tooth pain: DT, drug therapy
human
review
*acetylsalicylic acid: AE, . . .
RN (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6,
63781-77-1; (prostaglandin synthase) 39391-18-9, 59763-19-8, 9055-65-6;
(celecoxib) 169590-42-5; (rofecoxib) 162011-90-7, 186912-82-3;
(indometacin) 53-86-1, 74252-25-8, 7681-54-1; (diclofenac) 15307-79-6,
15307-86-5; (piroxicam) 36322-90-4; (ibuprofen) 15687-27-1; (etodolac)
41340-25-4; (meloxicam) 71125-38-7; (nimesulide) 51803-78-2; . . .

L11 ANSWER 5 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

AB Background: It is just 100 years since the introduction of aspirin to medicine. Since then, aspirin and its derivatives have been joined by acetaminophen, and the nonsteroidal anti-inflammatory drugs-ibuprofen, naproxen sodium, and ketoprofen-as the only over-the-counter (OTC) agents approved by the US Food and Drug Administration for the short-term treatment of pain, headache, dysmenorrhea, and fever. Recently the prescription use of aspirin has expanded to include a number of antiplatelet indications. Objective: The purpose of this paper is to review critically the history, mechanisms of action, efficacy, and tolerability of OTC analgesic and antipyretic products. Relatively new and potential future indications for these drugs are also discussed.

Conclusion: Although all of the OTC analgesic/antipyretic agents seem to share a common mechanism of prostaglandin inhibition, there are important differences in their pharmacology, efficacy, and side-effect profiles. Considering their often- unsupervised use, the risk-benefit ratio of this class of drugs has been extremely favorable. However, when used inappropriately, even these drugs pose significant risks to certain patient populations.

AN 2000237077 EMBASE

TI Over-the-counter analgesics and antipyretics: A critical assessment.

AU Hersh E.V.; Moore P.A.; Ross G.L.

CS Dr. E.V. Hersh, School of Dental Medicine, University of Pennsylvania,
4001 Spruce Street, Philadelphia, PA 19104-6003, United States

SO Clinical Therapeutics, (2000) 22/5 (500-548).
Refs: 264
ISSN: 0149-2918 CODEN: CLTHDG

CY United States
DT Journal; General Review
FS 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LA English
SL English
SO Clinical Therapeutics, (2000) 22/5 (500-548).
Refs: 264
ISSN: 0149-2918 CODEN: CLTHDG
AB . . . the only over-the-counter (OTC) agents approved by the US Food and Drug Administration for the short-term treatment of pain, headache, **dysmenorrhea**, and fever. Recently the prescription use of aspirin has expanded to include a number of antiplatelet indications. Objective: The purpose. . .
RN. . . (diflunisal) 22494-42-4; (fenoprofen) 29679-58-1, 31879-05-7, 34691-31-1; (sulindac) 38194-50-2; (indometacin) 53-86-1, 74252-25-8, 7681-54-1; (piroxicam) 36322-90-4; (tolmetin) 26171-23-3, 35711-34-3; (azapropazone) 13539-59-8; (celecoxib) **169590-42-5**; (rofecoxib) 162011-90-7, 186912-82-3; (caffeine) 30388-07-9, 58-08-2; (excedrin) 53908-21-7; (pseudoephedrine plus triprolidine) 8054-27-1; (guaifenesin) 93-14-1; (codeine) 76-57-3; (hydrocodone) 125-29-1, 25968-91-6, 34366-67-1; . . .

L11 ANSWER 6 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AB The authors made a review on dysmenorrhoea, with emphasys on physiopathology, diagnosis and treatment.
AN 2000215836 EMBASE
TI [Dysmenorrhoea].
DISMENORREIA.
AU Da Motta E.V.; Salomao A.J.; De Oliveira Ramos L.
CS E.V. Da Motta, Rua Campos Bicudo, 87, CEP 04536-010 SP, Brazil
SO Revista Brasileira de Medicina, (2000) 57/5 (369-386).
Refs: 55
ISSN: 0034-7264 CODEN: RBMEAU
CY Brazil
DT Journal; General Review
FS 005 General Pathology and Pathological Anatomy
010 Obstetrics and Gynecology
037 Drug Literature Index
LA Portuguese
SL English; Portuguese
SO Revista Brasileira de Medicina, (2000) 57/5 (369-386).
Refs: 55
ISSN: 0034-7264 CODEN: RBMEAU
CT Medical Descriptors:
***dysmenorrhea**: DI, diagnosis
***dysmenorrhea**: DT, drug therapy
***dysmenorrhea**: ET, etiology
***dysmenorrhea**: TH, therapy
pathophysiology
disease classification
anamnesis
differential diagnosis
hormonal therapy
acupuncture
transcutaneous nerve stimulation
neurectomy
hysterectomy

social support
human
review
*prostaglandin: EC, endogenous compound
*nonsteroid antiinflammatory agent: DT, drug therapy
*oral contraceptive agent: DT, . . .
RN. . . 363-24-6; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4,
53664-49-6, 63781-77-1; (naproxen) 22204-53-1, 26159-34-2; (indometacin)
53-86-1, 74252-25-8, 7681-54-1; (piroxicam) 36322-90-4; (ibuprofen)
15687-27-1; (celecoxib) **169590-42-5**; (rofecoxib) 162011-90-7,
186912-82-3; (ketoprofen) 22071-15-4, 57495-14-4; (mefenamic acid)
61-68-7; (diclofenac) 15307-79-6, 15307-86-5; (phenylbutazone) 129-18-0,
50-33-9, 8054-70-4; (meloxicam) 71125-38-7; (nimesulide) 51803-78-2; . . .

L11 ANSWER 7 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2000024413 EMBASE
TI Update on COX-2 inhibitors [2].
AU Mandell B.F.
CS B.F. Mandell, Dept. of Rheumatic/Immunologic Dis., Cleveland Clinic,
Cleveland, OH, United States
SO Cleveland Clinic Journal of Medicine, (2000) 67/1 (67).
ISSN: 0891-1150 CODEN: CCJMEL
CY United States
DT Journal; Letter
FS 006 Internal Medicine
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SO Cleveland Clinic Journal of Medicine, (2000) 67/1 (67).
ISSN: 0891-1150 CODEN: CCJMEL
CT Medical Descriptors:
*osteoarthritis: DT, drug therapy
*dysmenorrhea: DT, drug therapy
edema: SI, side effect
drug megadose
international standard unit
bleeding: SI, side effect
kidney failure
liver failure
bronchospasm
human
letter
*cyclooxygenase 2 inhibitor: AE, adverse drug. . .
RN (rofecoxib) 162011-90-7, 186912-82-3; (celecoxib) **169590-42-5**;
(warfarin) 129-06-6, 2610-86-8, 3324-63-8, 5543-58-8, 81-81-2

L11 ANSWER 8 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AB Identification of two isoforms of cyclooxygenase, COX-1 and COX-2, has
initiated a revolution in the approach to pharmacologic pain management.
It has been further determined that inhibition of COX-2 reduces
inflammation, and inhibition of COX-1 compromises gastrointestinal
mucosal
integrity. As traditional nonsteroidal anti-inflammatory drugs (NSAIDs)
inhibit both COX-1 and COX-2, gastrointestinal ulceration can develop in
association with the use of these agents to control pain and
inflammation.
An ideal NSAID would, therefore, inhibit COX-2 to provide
anti-inflammatory effects while leaving COX-1, and, therefore,

gastrointestinal mucosa, unaffected. Two selective COX-2 inhibitors have recently been approved in the United States. Celecoxib (Celebrex.RTM., G.D. Searle and Co.) and rofecoxib (Vioxx.RTM., Merck and Co., Inc.) are indicated for the treatment of osteoarthritis. Also, celecoxib is approved

for rheumatoid arthritis. Rofecoxib is also approved for the treatment of acute pain and **dysmenorrhea**. Both agents have displayed similar efficacy to traditional NSAIDs. In addition, endoscopically detected gastrointestinal ulceration is reduced versus older NSAIDs. Further evaluation of selective COX-2 inhibitors will elucidate long-term efficacy, safety, and potential reduction of health care dollars spent on hospitalization and treatment for NSAID-induced gastrointestinal toxicity.

AN 2000020809 EMBASE

TI Evaluation of novel new NSAIDs: A review of COX-2 inhibitors, with an emphasis on gastrointestinal toxicity.

AU Kirk J.K.; Hamilton J.M.; Phelps K.C.

CS J.K. Kirk, Dept. of Family and Community Med., Wake Forest University, School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157-1084, United States

SO Journal of Pharmacy Practice, (1999) 12/5 (401-411).

Refs: 42

ISSN: 0897-1900 CODEN: JPPREU

CY United States

DT Journal; General Review

FS 031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles

LA English

SL English

SO Journal of Pharmacy Practice, (1999) 12/5 (401-411).

Refs: 42

ISSN: 0897-1900 CODEN: JPPREU

AB . . . of osteoarthritis. Also, celecoxib is approved for rheumatoid arthritis. Rofecoxib is also approved for the treatment of acute pain and **dysmenorrhea**. Both agents have displayed similar efficacy to traditional NSAIDs. In addition, endoscopically detected gastrointestinal ulceration is reduced versus older NSAIDs.. . .

RN (celecoxib) 169590-42-5; (rofecoxib) 162011-90-7, 186912-82-3;
(meloxicam) 71125-38-7

L11 ANSWER 9 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

AN 1999394288 EMBASE

TI Quarterly drug-approval update: Hits and misses.

AU Goldenberg M.M.

CS Dr. M.M. Goldenberg, Clinical Product Development, Mgmt. Healthcare Associates, Inc., Florham Park, NJ, United States

SO P and T, (1999) 24/10 (480-489).

ISSN: 1052-1372 CODEN: PPTTEK

CY United States

DT Journal; General Review

FS 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LA English

SO P and T, (1999) 24/10 (480-489).

ISSN: 1052-1372 CODEN: PPTTEK

CT Medical Descriptors:

*drug . . . the curve

thrombosis: SI, side effect

solid tumor: DT, drug therapy
anemia: SI, side effect
cardiotoxicity: SI, side effect
obesity: DT, drug therapy
osteoarthritis: DT, drug therapy
dysmenorrhea: DT, drug therapy
pain: DT, drug therapy
non insulin dependent diabetes mellitus: DT, drug therapy
meningitis: DT, drug therapy
rheumatoid arthritis: DT, drug therapy
bleeding: . . .
RN (tetrahydrolipstatin) 96829-58-2; (rosiglitazone) 122320-73-4;
(cytarabine) 147-94-4, 69-74-9; (celecoxib) **169590-42-5**;
(doxorubicin) 23214-92-8, 25316-40-9; (triacylglycerol lipase) 9001-62-1;
(cytochrome p450) 9035-51-2; (rifampicin) 13292-46-1; (ibuprofen)
15687-27-1; (diclofenac) 15307-79-6, 15307-86-5; (insulin) 9004-10-8;
(hemoglobin alc). . .

L11 ANSWER 10 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

AB Pain is a common complaint, often occurring in conjunction with inflammation. Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most commonly used analgesic agents in ambulatory patients. In recent studies, the cyclooxygenase-2 (COX-2) inhibitor rofecoxib demonstrated analgesic effects similar to those of NSAIDs in the treatment of acute pain and primary **dysmenorrhea**. The present randomized, single-dose, double-blind, double-dummy, placebo- and active-comparator-controlled, parallel-group study was undertaken to compare the analgesic efficacy of the COX-2 inhibitors rofecoxib 50 mg and celecoxib 200 mg with that of ibuprofen 400 mg and placebo in patients with postoperative dental pain. Two hundred and seventy- two patients experiencing pain after the removal of .gtoreq.2 third molars were randomized according to pain severity (moderate vs severe) to receive a single dose of placebo (n = 45), rofecoxib 50 mg (n = 90), celecoxib 200 mg (n = 91), or ibuprofen 400 mg (n = 46). Using a patient diary, patients recorded pain intensity, pain relief, and global evaluations throughout the 24-hour period after dosing.

The overall analgesic effect, onset of action, peak effect, and duration of effect were evaluated, with the primary end point being total pain relief over 8 hours (TOPAR8). The safety profile was assessed on the basis

of physical findings, laboratory results, and spontaneous reports of adverse experiences. The results showed that compared with celecoxib, rofecoxib had superior analgesic effects on all measures of analgesic efficacy, including overall analgesic effect (TOPAR8, 18.3 vs 12.5; P < 0.001), time to onset of effect (30 vs 60 minutes; P = 0.003), peak pain relief (score, 2.8 vs 2.3; P < 0.05), and duration of effect (>24 vs 5.1 hours; P < 0.001). In addition, rofecoxib's analgesic efficacy was

similar to that of ibuprofen (TOPAR8, 18.3 vs 17.0; P = 0.460), but the duration was longer (P < 0.05); with ibuprofen, the time to on-set was 24 minutes,

peak pain relief score was 2.9, and duration of analgesic effect was 8.9 hours. The safety profile was similar across all treatment groups. Thus rofecoxib provided analgesic efficacy superior to that of celecoxib and comparable to that of ibuprofen in the treatment of patients with acute postoperative dental pain.

AN 1999389473 EMBASE

TI Comparison of rofecoxib and celecoxib, two cyclooxygenase-2 inhibitors, in postoperative dental pain: A randomized, placebo- and active-comparator-

controlled clinical trial.

AU Malmstrom K.; Daniels S.; Kotey P.; Seidenberg B.C.; Desjardins P.J.
CS Dr. K. Malmstrom, Maildrop RY32-621, 126 East Lincoln Avenue, Rahway, NJ
07065, United States

SO Clinical Therapeutics, (1999) 21/10 (1653-1663).
Refs: 24
ISSN: 0149-2918 CODEN: CLTHDG

CY United States
DT Journal; Article

FS 011 Otorhinolaryngology
024 Anesthesiology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LA English
SL English
SO Clinical Therapeutics, (1999) 21/10 (1653-1663).
Refs: 24
ISSN: 0149-2918 CODEN: CLTHDG

AB . . . cyclooxygenase-2 (COX-2) inhibitor rofecoxib demonstrated analgesic effects similar to those of NSAIDs in the treatment of acute pain and primary **dysmenorrhea**. The present randomized, single-dose, double-blind, double-dummy, placebo- and active-comparator-controlled, parallel-group study was undertaken to compare the analgesic efficacy of. . .

RN (celecoxib) 169590-42-5; (ibuprofen) 15687-27-1; (paracetamol) 103-90-2; (hydrocodone bitartrate) 143-71-5, 8013-91-0

L11 ANSWER 11 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 1999381366 EMBASE
TI Understanding xenical and vioxx.
AU Sisca T.
SO American Druggist, (1999) 216/10 (52-55).
ISSN: 0190-5279 CODEN: AMDRAG

CY United States
DT Journal; General Review

FS 006 Internal Medicine
010 Obstetrics and Gynecology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles

LA English
SO American Druggist, (1999) 216/10 (52-55).
ISSN: 0190-5279 CODEN: AMDRAG

CT Medical Descriptors:
*obesity: DT, drug therapy
*osteoarthritis: DT, drug therapy
***dysmenorrhea**: DT, drug therapy
gastrointestinal symptom: SI, side effect
drug efficacy
drug metabolism
drug mechanism
drug blood level
headache: SI, side effect
nausea: SI, side effect
dyspepsia: SI, side. . .

RN . . . 29122-68-7; (methotrexate) 15475-56-6, 59-05-2, 7413-34-5;
(cimetidine) 51481-61-9, 70059-30-2; (lithium carbonate) 554-13-2;
(rifampicin) 13292-46-1; (ketoconazole) 65277-42-1; (prednisone) 53-03-2;
(pravastatin) 81131-74-0; (celecoxib) 169590-42-5

=> s 57-63-6/rn and dysmenorrhea
 'RN' IS NOT A VALID FIELD CODE
 'RN' IS NOT A VALID FIELD CODE
 'RN' IS NOT A VALID FIELD CODE
 L12 26 57-63-6/RN AND DYSMENORRHEA

=> s l12 and py<2001
 3 FILES SEARCHED...
 L13 21 L12 AND PY<2001

=> dup rem l13
 PROCESSING COMPLETED FOR L13
 L14 21 DUP REM L13 (0 DUPLICATES REMOVED)

=> d l14 ab bib kwic

L14 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2002 ACS
 AB This invention concerns cyclic combination therapies using indoline
 derivs., which are progesterone receptor antagonists, or a
 pharmaceutically acceptable salt thereof. These methods may be used for
 contraception or treatment and/or prevention of secondary amenorrhea,
 dysfunctional bleeding, uterine leiomyomata, endometriosis; polycystic
 ovary syndrome, carcinomas and adenocarcinomas of the endometrium, ovary,
 breast, colon, prostate, or minimization of side effects or cyclic
 menstrual bleeding. Addnl. uses of the invention include stimulation of
 food intake. For example, 6-(3-chlorophenyl)-4,4-dimethyl-1,4-dihydro-3-
 oxa-1,8-diaza-naphthalene-2-one was prep'd. and tested in the range of
 0.01 nM to 5 .mu.M in the in vitro assays and 0.001-300 mg/kg in the in vivo
 assays.
 AN 2000:790292 CAPLUS
 DN 133:330061
 TI Cyclic regimens using cyclic urea and cyclic amide derivatives
 IN Grubb, Gary S.; Zhi, Lin; Jones, Todd K.; Tegley, Christopher M.; Puwen,
 Zhang; Fensome, Andrew; Viet, Andrew Q.; Santilli, Arthur A.; Terefenko,
 Eugene A.; Wrobel, Jay E.; Edwards, James P.
 PA American Home Products Corporation, USA; Ligand Pharmaceuticals, Inc.
 SO PCT Int. Appl., 61 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000066103	A2	20001109	WO 2000-US11449	20000501 <--
	WO 2000066103	A3	20010405		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	US 6399593	B1	20020604	US 2000-552037	20000419
	EP 1173208	A2	20020123	EP 2000-928519	20000501
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,			

IE, SI, LT, LV, FI, RO
 PRAI US 1999-198238P P 19990504
 US 2000-552037 A1 20000419
 WO 2000-US11449 W 20000501
 OS MARPAT 133:330061
 PI WO 2000066103 A2 20001109
 PATENT NO. KIND DATE APPLICATION NO. DATE
 ----- ----- ----- -----
 PI WO 2000066103 A2 20001109 WO 2000-US11449 20000501 <--
 WO 2000066103 A3 20010405
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
 CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
 ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
 LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
 SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
 ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 US 6399593 B1 20020604 US 2000-552037 20000419
 EP 1173208 A2 20020123 EP 2000-928519 20000501
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO
 IT **Dysmenorrhea**
 (cyclic urea and cyclic amide derivs. for oral contraception or
 treatment and prevention of various cancers and other disorders)
 IT 51-98-9, Norethindrone acetate 57-63-6, Ethinyl estradiol
 68-22-4, Norethindrone 427-51-0, Cyproterone acetate 797-63-7,
 Levonorgestrel 6533-00-2, Norgestrel 35189-28-7, Norgestimate
 53016-31-2, (17-Deacetyl)norgestimate 54024-22-5, Desogestrel
 54048-10-1, 3-Ketodesogestrel 58691-88-6, Nomegestrol 60282-87-3,
 Gestodene 65928-58-7, Dienogest 67392-87-4, Drospirenone
 74513-62-5,
 Trimegestone 105149-04-0, Osaterone
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological study);
 USES
 (Uses)
 (combinations with; cyclic urea and cyclic amide derivs. for oral
 contraception or treatment and prevention of various cancers and other
 disorders)

=> d 114 2-21 ab bib kwic

L14 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2002 ACS
 AB Objective: This is a randomized clin. trial comparing estroprogestin
 (E/P)
 pill given for 12 mo vs. gonadotropin releasing hormone agonist (GNRHa)
 given for 4 mo followed by E/P pill treatment for 8 mo in the relief of
 endometriosis-related pelvic pain. Methods: Eligible for the study were
 women with laparoscopically confirmed endometriosis and pelvic pain
 lasting 3-12 mo after diagnosis. Eligible women were randomly assigned
 to
 treatment with E/P pill (gestroden 0.75 mg and ethinylestradiol 0.03 mg)
 for 12 mo (47 patients) vs. triptorelin 3.75 mg slow release every 28
 days
 for 4 mo followed by E/P pill for 8 mo (55 patients). Results: At
 baseline, **dysmenorrhea** was reported in 46 women allocated to E/P

pill only (97.9%), and in all the 55 women allocated to GNRHa+E/P pill. The corresponding value at the 12 mo follow-up visit was 14 subjects (35.9%) and 16 subjects (34.8%). The baseline median values of the multidimensional and analog scale were for **dysmenorrhea** 4 and 6 in the EP only and 3 and 6 in the GNRHa+E/P group. The corresponding value at the 12 mo follow-up visit were 2 and 6 and 0 and 5. Non-menstrual pain was reported, resp., at baseline and 12 mo visit by 46 (97.9%) and 15 (38.5%) subjects in the E/P pill group and 49 (89.1%) and 17 (37.0%) of the GNRHa+E/P pill one. The baseline median values of the multidimensional and analog scale were for non-menstrual pain 3 and 5 in the E/P only and 2 and 6 in the GNRHa+E/P group. The corresponding values

at the 12 mo follow-up visit were 0 and 4 and 0 and 4. These differences between the two groups were not statistically significant. Conclusions:

1 of yr after randomization, the two treatment schedules show similar relief
of pelvic pain in women with endometriosis.

AN 2000:29941 CAPLUS
DN 132:59370

TI Estropiogestin vs. gonadotropin agonists plus estropiogestin in the treatment of endometriosis-related pelvic pain: a randomized trial

AU Parazzini, Fabio; Di Cintio, Elisabetta; Chatenoud, Liliane; Moroni, Simona; Ardovino, Italo; Struzziero, Elisario; Falsetti, Leopoldo; Bianchi, Albino; Bracco, Gianluca; Pellegrini, Alessandra; Bertulessi, Carlo; Romanini, Carlo; Zupi, Errico; Massobrio, Marco; Guidetti, Daniela;

Troiano, Luigi; Beretta, Paolo; Franchi, Massimo

CS Gruppo Italiano per lo Studio dell'Endometriosi, Prima Clinica Ostetrico Ginecologica, Universita di Milano, Milan, Italy

SO European Journal of Obstetrics & Gynecology and Reproductive Biology (2000), 88(1), 11-14

CODEN: EOGRAL; ISSN: 0301-2115

PB Elsevier Science Ireland Ltd.

DT Journal

LA English

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

SO European Journal of Obstetrics & Gynecology and Reproductive Biology (2000), 88(1), 11-14

CODEN: EOGRAL; ISSN: 0301-2115

AB Objective: This is a randomized clin. trial comparing estropiogestin (E/P)

pill given for 12 mo vs. gonadotropin releasing hormone agonist (GNRHa) given for 4 mo followed by E/P pill treatment for 8 mo in the relief of endometriosis-related pelvic pain. Methods: Eligible for the study were women with laparoscopically confirmed endometriosis and pelvic pain lasting 3-12 mo after diagnosis. Eligible women were randomly assigned

to treatment with E/P pill (gestroden 0.75 mg and ethinylestradiol 0.03 mg) for 12 mo (47 patients) vs. triptorelin 3.75 mg slow release every 28 days

for 4 mo followed by E/P pill for 8 mo (55 patients). Results: At baseline, **dysmenorrhea** was reported in 46 women allocated to E/P pill only (97.9%), and in all the 55 women allocated to GNRHa+E/P pill. The corresponding value at the 12 mo follow-up visit was 14 subjects (35.9%) and 16 subjects (34.8%). The baseline median values of the multidimensional and analog scale were for **dysmenorrhea** 4 and 6 in the EP only and 3 and 6 in the GNRHa+E/P group. The corresponding value at the 12 mo follow-up visit were 2 and 6 and 0 and 5.

Non-menstrual pain was reported, resp., at baseline and 12 mo visit by 46 (97.9%) and 15 (38.5%) subjects in the E/P pill group and 49 (89.1%) and 17 (37.0%) of the GNRHa+E/P pill one. The baseline median values of the multidimensional and analog scale were for non-menstrual pain 3 and 5 in the E/P only and 2 and 6 in the GNRHa+E/P group. The corresponding values

at the 12 mo follow-up visit were 0 and 4 and 0 and 4. These differences between the two groups were not statistically significant. Conclusions:

1 yr after randomization, the two treatment schedules show similar relief
of

, pelvic pain in women with endometriosis.

IT 57-63-6, Ethinylestradiol 57773-63-4, Triptorelin
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study);
USES

(Uses)

(estropogestin vs. gonadotropin agonists plus estropogestin in
treatment of endometriosis-related pelvic pain in humans)

L14 ANSWER 3 OF 21 USPATFULL

AB A method and kit for measurement of a steroid by means of a competitive
immunoassay, preferably a competitive enzyme immunoassay. The method
and

kit involve the use of a steroid analogue conjugated to a label. The
steroids that are amenable to detection by the method and kit of the
present invention include estradiol and progesterone. The method
comprises the steps of:

- given
- a. incubating a mixture of a test sample suspected of containing a steroid, a solid phase coupled to an antibody specific for that steroid, and a conjugate of an analogue of that steroid to form steroid/antibody complexes and conjugate/antibody complexes on said solid phase;
 - b. separating said solid phase from said mixture;
 - c. measuring the amount of label present in said mixture or in said solid phase; and
 - d. determining the amount of steroid in said sample from the amount of label. The kit comprises a solid phase coupled to an antibody specific for a steroid and a conjugate of an analogue of that steroid.

AN 1999:89008 USPATFULL

TI Determination of steroids by competitive immunoassay

IN Williams, Gregg T., Villa Park, IL, United States

Groskopf, William R., Libertyville, IL, United States

Baker, Harold N., Libertyville, IL, United States

Agdeppa, Dalmacio A., Morton Grove, IL, United States

PA Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation)

PI US 5932431 19990803 <--

AI US 1997-840782 19970416 (8)

RLI Division of Ser. No. US 1995-398226, filed on 3 Mar 1995, now patented,
Pat. No. US 5663054

DT Utility

FS Granted

EXNAM Primary Examiner: Huff, Sheela

LREP Weinstein, David L.

CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 1295

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5932431 19990803 <--
SUMM The measurement of estradiol is important for the evaluation of normal sexual development (menarche), causes of infertility (anovulation, amenorrhea, **dysmenorrhea**), and menopause. Normal estradiol levels are lowest at menses and during the early follicular phase

(25-75

pg/mL). The levels rise. . .

IT 50-27-1, Estriol 50-28-2, Estradiol, analysis 53-16-7, Estrone, analysis 57-63-6, Ethynodiol, analysis 57-83-0, Progesterone, analysis 57-91-0, 17.alpha.-Estradiol 58-22-0, Testosterone 68-96-2, 17-Hydroxyprogesterone 145-14-2, 20.alpha.-Hydroxyprogesterone (steroid detn. by competitive immunoassay)

L14 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2002 ACS

AB The efficacy and safety of the new, low dose, 21-day combination oral contraceptive Valette contg. 30 .mu.g of ethynodiol and 2 mg of dienogest was evaluated in a prospective six-cycle, open-label, multicenter postmarketing surveillance study. A total of 16,267 women were enrolled and had 92,146 documented cycles of exposure. Eleven pregnancies occurred during treatment, the unadjusted Pearl Index being 0.14. Of these, at least four pregnancies were obsd. in women with

intake

failures. A total of 333 (2.0%) women stopped Valette before the end of the observational period and withdrew from the study for nonmedical reasons, 1,563 (9.6%) for medical reasons, and 100 (0.61%) without giving any reason. The incidence of breakthrough bleeding and spotting were highest in the first treatment cycle (5.0 and 3.4%, resp.) and then declined rapidly to a very low level. The rate of withdrawal bleeding (silent menstruation) was about 2% throughout the study, affecting 5.9%

of

all women. The most commonly reported adverse events in this study which were considered at least possibly drug related were mastalgia (1.5%), wt. gain (1.1%), headache (1.1%), nausea/vomiting (1.0%), **dysmenorrhea** (0.35%), decreased libido (0.32%) depressive state (0.29%) and nonspecific

abdominal pain (0.14%), the incidence being therefore very low. This formulation provides a very high contraceptive efficacy in routine practice with excellent cycle control, tolerability and compliance as indicated in preceding clin. phase III studies.

AN 1999:506290 CAPLUS

DN 131:165426

TI Efficacy and tolerability of the dienogest-containing oral contraceptive Valette. Results of a postmarketing surveillance study

AU Zimmermann, T.; Dietrich, H.; Wisser, K.-H.; Hoffmann, H.

CS Dept. of Medical Affairs, Jenapharm GmbH and Co. KG, Jena, D-07745, Germany

SO Drugs of Today (1999), 35(Suppl. C), 79-87
CODEN: MDACAP; ISSN: 0025-7656

PB Prous Science

DT Journal

LA English

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

SO Drugs of Today (1999), 35(Suppl. C), 79-87

CODEN: MDACAP; ISSN: 0025-7656

AB The efficacy and safety of the new, low dose, 21-day combination oral contraceptive Valette contg. 30 .mu.g of ethinylestradiol and 2 mg of dienogest was evaluated in a prospective six-cycle, open-label, multicenter postmarketing surveillance study. A total of 16,267 women were enrolled and had 92,146 documented cycles of exposure. Eleven pregnancies occurred during treatment, the unadjusted Pearl Index being 0.14. Of these, at least four pregnancies were obsd. in women with intake failures. A total of 333 (2.0%) women stopped Valette before the end of the observational period and withdrew from the study for nonmedical reasons, 1,563 (9.6%) for medical reasons, and 100 (0.61%) without giving any reason. The incidence of breakthrough bleeding and spotting were highest in the first treatment cycle (5.0 and 3.4%, resp.) and then declined rapidly to a very low level. The rate of withdrawal bleeding (silent menstruation) was about 2% throughout the study, affecting 5.9% of all women. The most commonly reported adverse events in this study which were considered at least possibly drug related were mastalgia (1.5%), wt. gain (1.1%), headache (1.1%), nausea/vomiting (1.0%), **dysmenorrhea** (0.35%), decreased libido (0.32%) depressive state (0.29%) and nonspecific abdominal pain (0.14%), the incidence being therefore very low. This formulation provides a very high contraceptive efficacy in routine practice with excellent cycle control, tolerability and compliance as indicated in preceding clin. phase III studies.

IT 57-63-6, Ethinylestradiol 65928-58-7, Dienogest 170475-05-5, Valette
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy and tolerability of dienogest-contg. oral contraceptive Valette)

L14 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2002 ACS

AB A review with 62 refs. The reliable contraceptive effects of the combination drug Valette contg. 0.03 mg ethinylestradiol and 2.0 mg dienogest were confirmed by the results of a phase III study which revealed an unadjusted Pearl Index of 0.68 and an adjusted Pearl Index of 0.21. Calcns. according to the life-table method revealed a cumulative failure rate of 0.0052 after six cycles, of 0.0076 after 12 cycles, and of 0.0089 after 18 and 22 cycles of treatment. These data demonstrate that the efficacy of the ethinylestradiol-dienogest combination is comparable to that of other monophasic low dose oral contraceptives contg. 0.03 mg ethinylestradiol. They also confirm previous observations that the failure rate of oral contraception is highest during the first year of use. Similar to comparable low dose oral contraceptives, the use of ethinylestradiol and dienogest is assocd. with an increased rate of intermenstrual bleeding during the first cycle of treatment. Thereafter, the cycle control improves progressively, and after the third to fifth cycle, the rate of irregular bleeding is below that of pretreatment cycles. The proportion of women without withdrawal bleeding is small, and the strength and duration of this bleeding progressively decreases with time. Pretreatment **dysmenorrhea** also disappeared with increasing treatment cycles, demonstrating a therapeutic effect of this combination. No clin. relevant effects on various lab. parameters were obsd. Renin activity, angiotensin II, aldosterone, or endothelin-1 were unchanged, which might explain the lack of influence on blood pressure.

The levels of 3,5,3'-triiodothyronine (T3) and thyroxine (T4) increased significantly, those of free T3 (FT3) were only slightly elevated and those of free T4 (FT4) were reduced, while TSH (TSH) was not affected. There was no important influence of ethinylestradiol and dienogest on hematol. or other clin. lab. serum parameters; however, this drug combination caused slight hyperinsulinemia and insulin resistance. Glucose and HbA1c remained unaltered. The change in lipid metab. corresponds to the effects of other formulations with a predominance of the effect of the estrogen component. There was an increase in HDL-cholesterol, triglycerides, apolipoprotein A1 and B, but no change in LDL-cholesterol. The effects may be favorable rather than deleterious. The changes of hemostatic parameters were comparable to those obsd. with other oral contraceptives contg. a progestin with no or weak androgenic properties. For most of the procoagulatory, anticoagulatory and fibrinolytic parameters, the effects of the combination of ethinylestradiol and dienogest were equiv. to those of placebo.

AN 1999:506288 CAPLUS

DN 131:165345

TI Clinical findings with the dienogest-containing oral contraceptive
Valette

AU Moore, C.; Feichtinger, W.; Klinger, G.; Mellinger, U.; Spona, J.;
Walter,

F.; Winkler, U. H.; Zahradnik, H. P.

CS Dept. of Clinical Research, Jenapharm GmbH and Co. KG, Jena, D-07745,
Germany

SO Drugs of Today (1999), 35(Suppl. C), 53-68
CODEN: MDACAP; ISSN: 0025-7656

PB Prous Science

DT Journal; General Review

LA English

RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

SO Drugs of Today (1999), 35(Suppl. C), 53-68
CODEN: MDACAP; ISSN: 0025-7656

AB A review with 62 refs. The reliable contraceptive effects of the combination drug Valette contg. 0.03 mg ethinylestradiol and 2.0 mg dienogest were confirmed by the results of a phase III study which revealed an unadjusted Pearl Index of 0.68 and an adjusted Pearl Index of 0.21. Calcns. according to the life-table method revealed a cumulative failure rate of 0.0052 after six cycles, of 0.0076 after 12 cycles, and of

0.0089 after 18 and 22 cycles of treatment. These data demonstrate that the efficacy of the ethinylestradiol-dienogest combination is comparable to that of other monophasic low dose oral contraceptives contg. 0.03 mg ethinylestradiol. They also confirm previous observations that the failure rate of oral contraception is highest during the first year of use. Similar to comparable low dose oral contraceptives, the use of ethinylestradiol and dienogest is assocd. with an increased rate of intermenstrual bleeding during the first cycle of treatment. Thereafter, the cycle control improves progressively, and after the third to fifth cycle, the rate of irregular bleeding is below that of pretreatment cycles. The proportion of women without withdrawal bleeding is small,

and

the strength and duration of this bleeding progressively decreases with time. Pretreatment dysmenorrhea also disappeared with increasing treatment cycles, demonstrating a therapeutic effect of this combination. No clin. relevant effects on various lab. parameters were obsd. Renin activity, angiotensin II, aldosterone, or endothelin-1 were unchanged, which might explain the lack of influence on blood pressure. The levels of 3,5,3'-triiodothyronine (T3) and thyroxine (T4) increased

significantly, those of free T3 (FT3) were only slightly elevated and those of free T4 (FT4) were reduced, while TSH (TSH) was not affected. There was no important influence of ethinylestradiol and dienogest on hematol. or other clin. lab. serum parameters; however, this drug combination caused slight hyperinsulinemia and insulin resistance. Glucose and HbA1c remained unaltered. The change in lipid metab. corresponds to the effects of other formulations with a predominance of the effect of the estrogen component. There was an increase in HDL-cholesterol, triglycerides, apolipoprotein A1 and B, but no change in LDL-cholesterol. The effects may be favorable rather than deleterious. The changes of hemostatic parameters were comparable to those obsd. with other oral contraceptives contg. a progestin with no or weak androgenic properties. For most of the procoagulatory, anticoagulatory and fibrinolytic parameters, the effects of the combination of ethinylestradiol and dienogest were equiv. to those of placebo.

IT 57-63-6, Ethinylestradiol 65928-58-7, Dienogest
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clin. findings with dienogest-contg. oral contraceptive Valette)

L14 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2002 ACS

AB Patients with endometriosis were given gonadotropin-releasing hormone agonists (GnRHa) with or without hormone add-back therapy (+ 20 .mu.g of ethinyl estradiol with 0.15 mg desogestrel) designed to suppress the adverse effects of hypoestrogenism while preserving the efficacy of GnRHa.

Both regimens showed improvements in endometriosis, dysmenorrhea, and pelvic pain. Effects were better in the GnRHa + placebo group.

The GnRHa + placebo group had higher serum Ca levels and a higher loss of lumbar spine bone mineral d. (BMD). Urinary levels of pyridinium crosslinks increased in the GnRHa + placebo group, and declined to normal in the GnRHa + add-back group. The add-back therapy protects women taking

GnRHAs from severe loss of BMD and accelerated bone collagen resorption, but reduces the efficacy of the GnRHa.

AN 1999:43842 CAPLUS

DN 130:105471

TI Effects of add-back therapy on bone mineral density and pyridinium crosslinks in patients with endometriosis treated with gonadotropin-releasing hormone agonists

AU Gnoth, Christian; Goedtke, Katrin; Freundl, Guenter; Godehardt, Eberhardt;

Kienle, Erika

CS Dep. Gynecology Obstetrics, Academic Hospital, Univ. Duesseldorf, Duesseldorf, D-40593, Germany

SO Gynecologic and Obstetric Investigation (1999), 47(1), 37-41
CODEN: GOBIDS; ISSN: 0378-7346

PB S. Karger AG

DT Journal

LA English

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

SO Gynecologic and Obstetric Investigation (1999), 47(1), 37-41
CODEN: GOBIDS; ISSN: 0378-7346

AB Patients with endometriosis were given gonadotropin-releasing hormone agonists (GnRHa) with or without hormone add-back therapy (+ 20 .mu.g of ethinyl estradiol with 0.15 mg desogestrel) designed to suppress the adverse effects of hypoestrogenism while preserving the efficacy of GnRHa.

Both regimens showed improvements in endometriosis, **dysmenorrhea**, and pelvic pain. Effects were better in the GnRHa + placebo group.

The GnRHa + placebo group had higher serum Ca levels and a higher loss of lumbar spine bone mineral d. (BMD). Urinary levels of pyridinium crosslinks increased in the GnRHa + placebo group, and declined to normal in the GnRHa + add-back group. The add-back therapy protects women taking GnRHAs from severe loss of BMD and accelerated bone collagen resorption, but reduces the efficacy of the GnRHa.

IT 57-63-6, Ethinyl estradiol 54024-22-5, Desogestrel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(gonadotropin-releasing hormone agonists add-back therapy effect on bone mineral d. and pyridinium crosslinks in endometriosis)

L14 ANSWER 7 OF 21 USPATFULL

AB Sulfated benzothiophenes of the formula I ##STR1## wherein R.sup.1 is hydrogen, hydroxy, C.sub.1 -C.sub.4 alkoxy, --OCOO(C.sub.1 -C.sub.6 alkyl), --OCO(C.sub.1 -C.sub.6 alkyl), --OCOAr wherein Ar is phenyl or optionally substituted phenyl, --OSO.sub.2 (C.sub.4 -C.sub.6 straight chain alkyl), or --OSO.sub.3 H;
R.sup.2 is R.sup.1, Cl or F; with the proviso that at least one of R.sup.1 or R.sup.2 is --OSO.sub.3 H;
R.sup.3 is 1-piperidinyl, 1-pyrrolidinyl, methyl-1-pyrrolidinyl, dimethyl-1-pyrrolidino, 4-morpholino, dimethylamino, diethylamino, diisopropylamino, or 1-hexamethyleneimino; and
n is 2 or 3;
or a pharmaceutically acceptable salt or solvate thereof.

AN 1998:150986 USPATFULL

TI Sulfated benzothiophene derivatives, methods of use and formulations containing same

IN Clay, Michael Paul, Greenwood, IN, United States
Frolik, Charles Alan, Indianapolis, IN, United States
Jones, Charles David, Indianapolis, IN, United States
Lindstrom, Terry Donald, Indianapolis, IN, United States

PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)

PI US 5843984 19981201 <--
AI US 1997-843308 19970414 (8)
PRAI US 1996-17110P 19960509 (60)

DT Utility
FS Granted

EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Ngo, Tamthom T.
LREP Sales, James J., Boone, David E.

CLMN Number of Claims: 18

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1200

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5843984 19981201 <--
SUMM This condition is a cause of **dysmenorrhea** and infertility in women. The exact cause of this condition is poorly understood but

evidence suggests that it is an. . .

SUMM Endometriosis is a condition of severe **dysmenorrhea**, which is accompanied by severe pain, bleeding into the endometrial masses or peritoneal cavity and often leads to infertility. The. . .

IT 57-63-6, 17.alpha.-Ethynodiol 68-22-4, Norethindrone 68-23-5, Norethynodrel 71-58-9, Provera 72-33-3, Mestranol (formulations contg. sulfated benzothiophene derivs. and estrogen or progestin for treatment of post-menopausal disorders)

L14 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2002 ACS

AB The objective of the study was to compare the cycle control and tolerability of two oral contraceptives contg. 20 .mu.g ethinylestradiol and either 150 .mu.g desogestrel or 75 .mu.g gestodene. A randomized, multicenter study was conducted in which 1016 healthy adult women received the desogestrel (n = 509) or the gestodene (n = 507) prepn. for six treatment cycles. No significant differences in bleeding patterns were detected between the two treatments. The incidence and duration of irregular bleeding decreased markedly, and to a similar extent, during each treatment. The occurrence of irregular bleeding per cycle decreased from 24.6 to 9.4% in the desogestrel group and from 19.7 to 8.6% in the gestodene group. Its duration fell from 1.1 to 0.2 days and from 0.9 to 0.3 days, resp. There was a consistently low incidence of amenorrhea (1.0-2.8%). There were no significant differences between treatments for the incidence, intensity or emergence of **dysmenorrhea**. During both treatments, the incidence of premenstrual syndrome and complaints such as breast tenderness, nausea and headache dropped markedly. Ultra low-dose oral contraceptives contg. desogestrel or gestodene offer equiv., good cycle control and improvements in **dysmenorrhea** and premenstrual syndrome and have similar, excellent tolerability profiles.

AN 1999:242258 CAPLUS

DN 131:68234

TI A comparison of the cycle control and tolerability of two ultra low-dose oral contraceptives containing 20 .mu.g ethinylestradiol and either 150 .mu.g desogestrel or 75 .mu.g gestodene

AU Serfaty, D.; Vree, M. L.

CS Hospital Saint-Louis, Paris, 75475, Fr.

SO European Journal of Contraception & Reproductive Health Care (1998), 3(4), 179-189
CODEN: ECRCFK; ISSN: 1362-5187

PB Parthenon Publishing Group Ltd.

DT Journal

LA English

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

SO European Journal of Contraception & Reproductive Health Care (1998), 3(4), 179-189
CODEN: ECRCFK; ISSN: 1362-5187

AB The objective of the study was to compare the cycle control and tolerability of two oral contraceptives contg. 20 .mu.g ethinylestradiol and either 150 .mu.g desogestrel or 75 .mu.g gestodene. A randomized, multicenter study was conducted in which 1016 healthy adult women received the desogestrel (n = 509) or the gestodene (n = 507) prepn. for six treatment cycles. No significant differences in bleeding patterns were detected between the two treatments. The incidence and duration of irregular bleeding decreased markedly, and to a similar extent, during each treatment. The occurrence of irregular bleeding per cycle decreased from 24.6 to 9.4% in the desogestrel group and from 19.7 to 8.6% in the

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good cycle control and improvements in **dysmenorrhea** and premenstrual syndrome and have similar, excellent tolerability profiles.

IT Amenorrhea

Dysmenorrhea

Menstruation

(comparison of cycle control and tolerability of two ultra low dose oral contraceptives contg. 20 .mu.g ethinylestradiol and either 150 .mu.g desogestrel or 75 .mu.g gestodene)

IT 57-63-6, Ethynylestradiol 54024-22-5, Desogestrel 60282-87-3, Gestodene

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(comparison of cycle control and tolerability of two ultra low dose oral contraceptives contg. 20 .mu.g ethinylestradiol and either 150 .mu.g desogestrel or 75 .mu.g gestodene)

L14 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2002 ACS

AB The benefit of an add-back therapy combining leuprorelin acetate (LEP) with ethinylestradiol plus desogestrel was evaluated in the treatment of endometriosis. In group A, patients were treated with 3.75 mg LEP depot per mo i.m. in combination with 20 mg ethinylestradiol plus 0.15 mg desogestrel orally for 3 wk. In group P, patients received LEP, following

the same schedule as in group A, and placebo. Treatment duration was 6 mo. At 1st-look laparoscopy (postoperatively) group A had an r-AFS (revised guidelines of the American Fertility Society) score of 23.57 and group P of 24.23. After 6 mo of treatment with LEP depot r-AFS scores were 16.14 and 6.25 in group A and P, resp. at 2nd-look laparoscopy. Hypoestrogenic adverse drug reactions (e.g. hot flushes, sweating, and sleeplessness) were more frequently in group P, whereas headache was comparable in both groups. **Dysmenorrhea** was reduced in both groups. Dyspareunia decreased in group P. Loss of bone mineral d.

caused

by the gonadotropin-releasing hormone agonist was reduced by the combined estrogen/progestin add-back therapy.

AN 1998:323524 CAPLUS

DN 129:738

TI Steroidal add-back therapy in patients treated with GnRH agonists

AU Freundl, G.; Goedtke, K.; Gnoth, C.; Godehardt, E.; Kienle, E.

CS Dep. Gynaecology Obstetrics, Academic Hospital, Univ. Duesseldorf, Duesseldorf, D-40593, Germany

SO Gynecologic and Obstetric Investigation (1998), 45(Suppl. 1, Management in Gynecology: The Role of a GnRH-a, Leuprorelin Acetate Depot), 22-30

CODEN: GOBIDS; ISSN: 0378-7346

PB S. Karger AG

DT Journal

LA English

SO Gynecologic and Obstetric Investigation (1998), 45(Suppl. 1, Management in Gynecology: The Role of a GnRH-a, Leuprorelin Acetate Depot), 22-30

CODEN: GOBIDS; ISSN: 0378-7346

AB The benefit of an add-back therapy combining leuprorelin acetate (LEP)

with ethinyloestradiol plus desogestrel was evaluated in the treatment of endometriosis. In group A, patients were treated with 3.75 mg LEP depot per mo i.m. in combination with 20 mg ethinyloestradiol plus 0.15 mg desogestrel orally for 3 wk. In group P, patients received LEP, following

the same schedule as in group A, and placebo. Treatment duration was 6 mo. At 1st-look laparoscopy (postoperatively) group A had an r-AFS (revised guidelines of the American Fertility Society) score of 23.57 and group P of 24.23. After 6 mo of treatment with LEP depot r-AFS scores were 16.14 and 6.25 in group A and P, resp. at 2nd-look laparoscopy. Hypoestrogenic adverse drug reactions (e.g. hot flushes, sweating, and sleeplessness) were more frequently in group P, whereas headache was comparable in both groups. **Dysmenorrhea** was reduced in both groups. **Dyspareunia** decreased in group P. Loss of bone mineral d. caused

by the gonadotropin-releasing hormone agonist was reduced by the combined estrogen/progestin add-back therapy.

IT 57-63-6, Ethinyloestradiol 54024-22-5, Desogestrel 57773-63-4, Triptorelin 74381-53-6, Leuprorelin acetate 145781-92-6, Goserelin acetate

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study);

USES

(Uses)

(steroidal add-back therapy in patients treated with GnRH agonists)

L14 ANSWER 10 OF 21 USPATFULL

AB A method and kit for measurement of asteroid by means of a competitive immunoassay, preferably a competitive enzyme immunoassay. The method and

kit involve the use of asteroid analogue conjugated to a label. The steroids that are amenable to detection by the method and kit of the present invention include estradiol and progesterone.

The method comprises the steps of:

- given a. incubating a mixture of a test sample suspected of containing a steroid, a solid phase coupled to an antibody specific for that steroid, and a conjugate of an analogue of that steroid to form steroid/antibody complexes and conjugate/antibody complexes on said solid phase;
- b. separating said solid phase from said mixture;
- c. measuring the amount of label present in said mixture or in said solid phase; and
- d. determining the amount of steroid in said sample from the amount of label.

The kit comprises a solid phase coupled to an antibody specific for a steroid and a conjugate of an analogue of that steroid.

AN 97:78325 USPATFULL

TI Determination of steroids by competitive immunoassay

IN Williams, Gregg T., Villa Park, IL, United States

Groskopf, William R., Libertyville, IL, United States

Baker, Harold N., Libertyville, IL, United States

Agdeppa, Dalmacio A., Morton Grove, IL, United States

PA Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation)
PI US 5663054 19970902 <--
AI US 1995-398226 19950303 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Scheiner, Toni R.; Assistant Examiner: Huff, Sheela
J.
LREP Weinstein, David L.
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 1497
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5663054 19970902 <--
SUMM The measurement of estradiol is important for the evaluation of normal sexual development (menarche), causes of infertility (anovulation, amenorrhea, **dysmenorrhea**), and menopause. Normal estradiol levels are lowest at menses and during the early follicular phase
(25-75 pg/mL). The levels rise. . .
IT 50-27-1, Estriol 50-28-2, Estradiol, analysis 53-16-7, Estrone, analysis 57-63-6, Ethynodiol, analysis 57-83-0, Progesterone, analysis 57-91-0, 17.alpha.-Estradiol 58-22-0, Testosterone 68-96-2, 17-Hydroxyprogesterone 145-14-2,
20.alpha.-Hydroxyprogesterone
(steroid detn. by competitive immunoassay)
L14 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2002 ACS
AB The authors tested the hypothesis that extending the no. of consecutive active oral contraceptives (OC)s given will decrease the frequency of menstrual-related problems including **dysmenorrhea**, menorrhagia, premenstrual-type symptoms, and menstrual migraines. A prospective anal. was designed to track the experience of 50 women taking OCs and experiencing menstrual-related problems. Fifty consecutive patients, who were taking OCs and had symptoms during the pill-free interval, were followed in a multispecialty clinic by an individual physician and nurse practitioner team. The patients were permitted to extend the no. of consecutive active OCs to delay menstrual-related symptoms. Immediate outcome of the 50 patients revealed 74% (37 patients) stabilized on an extended regimen of 6 to 12 wk of consecutive days with active OCs. Twenty-six percent (13 patients) either discontinued OCs or returned to the std. regimen with 3 wk of active pills. Of the 37 patients who were stabilized on an extended regimen, 27 have completed thus far between five and 13 extended cycles with 6-23 mo of follow-up (mean 16 mo).
Experience in a series of 50 OC users with menstrual-related symptoms demonstrated that delaying menses by extending the no. of consecutive days of active pills is well tolerated and efficacious. The authors believe that a large prospective study is warranted to further our knowledge in this area.
AN 1997:129002 CAPLUS
DN 126:152933
TI Extending the duration of active oral contraceptive pills to manage hormone withdrawal symptoms
AU Sulak, Patricia J.; Cressman, Brian E.; Waldrop, Enid; Holleman, Sonia; Kuehl, Thomas J.
CS Department of Obstetrics, Scott and White Clinic and Memorial Hospital, Texas A and M University Health Science Center College of Medicine, Temple, TX, USA

SO Obstetrics and Gynecology (New York) (1997), 89(2), 179-183
CODEN: OBGNAS; ISSN: 0029-7844

PB Elsevier

DT Journal

LA English

SO Obstetrics and Gynecology (New York) (1997), 89(2), 179-183
CODEN: OBGNAS; ISSN: 0029-7844

AB The authors tested the hypothesis that extending the no. of consecutive active oral contraceptives (OC)s given will decrease the frequency of menstrual-related problems including **dysmenorrhea**, menorrhagia, premenstrual-type symptoms, and menstrual migraines. A prospective anal. was designed to track the experience of 50 women taking OCs and experiencing menstrual-related problems. Fifty consecutive patients, who were taking OCs and had symptoms during the pill-free interval, were followed in a multispecialty clinic by an individual physician and nurse practitioner team. The patients were permitted to extend the no. of consecutive active OCs to delay menstrual-related symptoms. Immediate outcome of the 50 patients revealed 74% (37 patients) stabilized on an extended regimen of 6 to 12 wk of consecutive days with active OCs. Twenty-six percent (13 patients) either discontinued OCs or returned to the std. regimen with 3 wk of active pills. Of the 37 patients who were stabilized on an extended regimen, 27 have completed thus far between five and 13 extended cycles with 6-23 mo of follow-up (mean 16 mo).

Experience in a series of 50 OC users with menstrual-related symptoms demonstrated that delaying menses by extending the no. of consecutive days of active pills is well tolerated and efficacious. The authors believe that a large prospective study is warranted to further our knowledge in this area.

IT **Dysmenorrhea**
Menstruation
 (extending duration of active oral contraceptive pills to manage hormone withdrawal symptoms in women)

IT 57-63-6, Ethinyl estradiol 68-22-4, Norethindrone 797-63-7
54024-22-5, Desogestrel
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (extending duration of active oral contraceptive pills to manage hormone withdrawal symptoms in women)

L14 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2002 ACS

AB Our purpose was to evaluate the efficacy and safety of depot medroxyprogesterone acetate vs. an oral contraceptive combined with very-low-dose danazol in the long-term treatment of pelvic pain in women with endometriosis. Eighty patients with endometriosis and moderate or severe pelvic pain were randomized to treatment for 1 yr with i.m. depot medroxyprogesterone acetate 150 mg every 3 mo or a cyclic monophasic oral contraceptive (ethinyl estradiol 0.02 mg, desogestrel 0.15 mg) combined with oral danazol 50 mg a day for 21 days of each 28-day cycle. The women were asked to grade the degree of their satisfaction at the end of therapy. Variations in severity of symptoms during treatment were detd. by a 10 cm visual analog and a 0- to 3-point verbal rating scale. Twenty nine of 40 subjects (72.5%) in the depot medroxyprogesterone acetate group were satisfied after 1 yr of therapy compared with 23 of 40 (57.5%) in the oral contraceptive plus danazol group ($\chi^2=1.37$, $p=0.24$, odds ratio 1.95, 95% confidence interval 0.76 to 4.97). A significant decrease was obsd. in all symptom scores in both study groups. At 1-yr assessment

be **dysmenorrhea** was significantly greater in women allocated to oral contraceptive plus danazol. Depot medroxyprogesterone acetate seems to be an effective, safe, and convenient low-cost treatment for pelvic pain assocd. with endometriosis. However, women should be carefully counseled regarding menstrual changes and the potential prolonged delay in the return of ovulation.

AN 1996:578711 CAPLUS

DN 125:238862

TI Depot medroxyprogesterone acetate versus an oral contraceptive combined with very-low-dose danazol for long-term treatment of pelvic pain associated with endometriosis

AU Vercellini, Paolo; De Giorgi, Olga; Oldani, Sabina; Cortesi, Ilenia; Panazza, Stefania; Crosignani, Pier Giorgio

CS Clinica Ostetrica e Ginecologica "Luigi Mangiagalli,", University Milano, Milan, 20122, Italy

SO American Journal of Obstetrics and Gynecology (1996), 175(2), 396-401
CODEN: AJOGAH; ISSN: 0002-9378

PB Mosby-Year Book

DT Journal

LA English

SO American Journal of Obstetrics and Gynecology (1996), 175(2), 396-401
CODEN: AJOGAH; ISSN: 0002-9378

AB Our purpose was to evaluate the efficacy and safety of depot medroxyprogesterone acetate vs. an oral contraceptive combined with very-low-dose danazol in the long-term treatment of pelvic pain in women with endometriosis. Eighty patients with endometriosis and moderate or severe pelvic pain were randomized to treatment for 1 yr with i.m. depot medroxyprogesterone acetate 150 mg every 3 mo or a cyclic monophasic oral contraceptive (ethinyl estradiol 0.02 mg, desogestrel 0.15 mg) combined with oral danazol 50 mg a day for 21 days of each 28-day cycle. The women were asked to grade the degree of their satisfaction at the end of therapy. Variations in severity of symptoms during treatment were detd. by a 10 cm visual analog and a 0- to 3-point verbal rating scale. Twenty nine of 40 subjects (72.5%) in the depot medroxyprogesterone acetate group were satisfied after 1 yr of therapy compared with 23 of 40 (57.5%) in the oral contraceptive plus danazol group ($\chi^2=1.37$, $p=0.24$, odds ratio 1.95, 95% confidence interval 0.76 to 4.97). A significant decrease was obsd. in all symptom scores in both study groups. At 1-yr assessment **dysmenorrhea** was significantly greater in women allocated to oral contraceptive plus danazol. Depot medroxyprogesterone acetate seems to be an effective, safe, and convenient low-cost treatment for pelvic pain assocd. with endometriosis. However, women should be carefully counseled regarding menstrual changes and the potential prolonged delay in the return of ovulation.

IT 57-63-6, Ethinyl estradiol 71-58-9, Depot medroxyprogesterone acetate 54024-22-5, Desogestrel
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(depot medroxyprogesterone acetate vs. an oral contraceptive combined with very-low-dose danazol for long-term treatment of pelvic pain

assocd. with endometriosis in humans)

L14 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2002 ACS

AB The aim of this study was to compare contraceptive reliability, cycle control and tolerance of an oral contraceptive contg. 20 .mu.g ethinylestradiol and 75 .mu.g gestodene, with a ref. prepn. contg. the same dose of estrogen combined with 150 .mu.g desogestrel. This article presents interim data from centers in France and Austria, involving a total of 479 women and 4,991 cycles. Contraceptive reliability was good with both preps. With respect to cycle control, there is a trend towards

a lower incidence of intermenstrual bleeding in the gestodene group. The incidence of spotting (scanty bleeding) during the important first three cycles was 3.5% lower in the gestodene group, and over the first six cycles, it was 7.6% lower. Amenorrhea was similar in both groups, but

the

incidence of **dysmenorrhea** was significantly lower in the gestodene group ($p = 0.001$). Adverse events were similar in both groups, with headache, breast tension and nausea the most frequently reported symptoms. Body wt. remained relatively const. during treatment in both groups, and no hypertension was reported for any woman during the course of the study. In each treatment group, 19 women discontinued because of adverse events. It is concluded that both preps. are reliable and well tolerated oral contraceptives; however, there is a more favorable effect on **dysmenorrhea** by the gestodene formulation.

AN 1995:940912 CAPLUS

DN 124:45916

TI A twelve-month comparative clinical investigation of two low-dose oral contraceptives containing 20 .mu.g ethinylestradiol/75 .mu.g gestodene and

20 .mu.g ethinylestradiol/150 .mu.g desogestrel, with respect to efficacy, cycle control and tolerance

AU Endrikat, J.; Jaques, M. -A.; Mayerhofer, M.; Pelissier, C.; Mueller, U.; Duesterberg, B.

CS Schering AG, Berlin, D-13342, Germany

SO Contraception (1995), 52(4), 229-35
CODEN: CCPTAY; ISSN: 0010-7824

PB Elsevier

DT Journal

LA English

SO Contraception (1995), 52(4), 229-35
CODEN: CCPTAY; ISSN: 0010-7824

AB The aim of this study was to compare contraceptive reliability, cycle control and tolerance of an oral contraceptive contg. 20 .mu.g ethinylestradiol and 75 .mu.g gestodene, with a ref. prepn. contg. the same dose of estrogen combined with 150 .mu.g desogestrel. This article presents interim data from centers in France and Austria, involving a total of 479 women and 4,991 cycles. Contraceptive reliability was good with both preps. With respect to cycle control, there is a trend towards

a lower incidence of intermenstrual bleeding in the gestodene group. The incidence of spotting (scanty bleeding) during the important first three cycles was 3.5% lower in the gestodene group, and over the first six cycles, it was 7.6% lower. Amenorrhea was similar in both groups, but

the

incidence of **dysmenorrhea** was significantly lower in the gestodene group ($p = 0.001$). Adverse events were similar in both groups, with headache, breast tension and nausea the most frequently reported symptoms. Body wt. remained relatively const. during treatment in both

groups, and no hypertension was reported for any woman during the course of the study. In each treatment group, 19 women discontinued because of adverse events. It is concluded that both preps. are reliable and well tolerated oral contraceptives; however, there is a more favorable effect on **dysmenorrhea** by the gestodene formulation.

IT 57-63-6, Ethinylestradiol 54024-22-5, Desogestrel 60282-87-3,
Gestodene
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy, cycle control and tolerance of low-dose oral contraceptives
contg. 20 .mu.g ethinylestradiol/75 .mu.g gestodene and 20 .mu.g
ethinylestradiol/150 .mu.g desogestrel in humans)

L14 ANSWER 14 OF 21 USPATFULL

AB The present invention relates to the measurement of estradiol using competitive immunoassay methods. The inventors unexpectedly discovered that estrone and its derivatives conjugated to a label is a particularly

effective tracer when used in conjunction with estradiol specific antibodies to determine estradiol levels in fluid samples. The present invention also utilizes 5.alpha.-dihydrotestosterone to enhance the assay performance.

AN 94:75442 USPATFULL

TI Determination of estradiol by competitive immunoassay

IN Baker, Harold N., Libertyville, IL, United States

Eng, Katherine K., Libertyville, IL, United States

Gurner, William D., Chicago, IL, United States

Massei, Michael K., Lake Villa, IL, United States

Necklaws: Elizabeth C., Grayslake, IL, United States

Osikowicz, Eugene W., Lake Zurich, IL, United States

Ramp, Sally K., Gurnee, IL, United States

Trach, Paula, Gurnee, IL, United States

PA Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation)

<--

PI US 5342760 19940830

AI US 1992-896269 19920610 (7)

DT Utility

FS Granted

EXNAM Primary Examiner: Ceperley, Mary E.

LREP Wong, Wean Khing

CLMN Number of Claims: 11

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 649

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5342760 19940830

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SUMM The measurement of estradiol is important for the evaluation of normal sexual development (menarche), causes of infertility (anovulation, amenorrhea, **dysmenorrhea**), and menopause. Normal estradiol levels are lowest at menses and during the early follicular phase

(25-75

pg/ml). The levels rise. . .

IT 50-27-1, Estriol 57-63-6, Ethinyl estradiol 15270-30-1,

Estradiol3-glucuronide

(cross-reaction of, in estradiol competitive immunoassay)

L14 ANSWER 15 OF 21 USPATFULL

AB Aqueous parenteral solutions of drugs which are insoluble or only sparingly soluble in water and/or which are unstable in water, combined with cyclodextrin selected from the group consisting of hydroxypropyl,

hydroxyethyl, glucosyl, maltosyl and maltotriosyl derivatives of
.beta.- and .gamma.-cyclodextrin, provide a means for alleviating problems
associated with drug precipitation at the injection site and/or in the
lungs or other organs following parenteral administration.

AN 91:48610 USPATFULL <--
TI Pharmaceutical formulations for parenteral use
IN Bodor, Nicholas S., Gainesville, FL, United States
PA University of Florida, Gainesville, FL, United States (U.S.
corporation)
PI US 5024998 19910618
AI US 1989-448655 19891211 (7)
DCD 20080108
RLI Continuation-in-part of Ser. No. US 1987-139755, filed on 30 Dec 1987
And a continuation-in-part of Ser. No. US 1988-174945, filed on 29 Mar
1988 And a continuation-in-part of Ser. No. US 1989-431222, filed on 3
Nov 1989 which is a continuation-in-part of Ser. No. 139755 And a
continuation-in-part of Ser. No. 174945 which is a
continuation-in-part of Ser. No. 139755
PRAI CA 1988-585791 19881213
IE 1988-3717 19881213
IE 1989-810 19890314
DT Utility
FS Granted
EXNAM Primary Examiner: Griffin, Ronald W.
LREP Baumeister, Mary Katherine
CLMN Number of Claims: 86
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 5098
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5024998 19910618 <--
DETD . . . ##STR49##
3-hydroxy-17.beta.-[(1-methyl-1,4-dihydropyridin-3-yl)carbonyl]-oxyestra-1,3,5(10)-triene estradiol-CDSor E.sub.2 -CDS
U.S. Pat. No. 4,617,298, Example 11 estrogen (e.g. for control of
menopausal symptoms, menstrual disorders such as dysmenorrhea
, as a contraceptive component, for weight control, for prostate cancer,
for male sexual dysfunction) ##STR50## 17.beta.-[(1-methyl-1,4-dihydropyridin-3-yl)carbonyl]oxy}pregn-4-en-20-yn-3-one
ethisterone-CDS
Brewster et al, Pharmaceutical Research (1986), 3(5), . . .
IT 50-02-2, Dexamethasone 50-06-6, Phenobarbital, biological studies
50-23-7, Hydrocortisone 50-24-8 50-27-1, Estriol 50-28-2,
17.beta.-Estradiol, biological studies 50-44-2, Mercaptopurine
50-47-5, Desipramine 50-50-0, Estradiol benzoate 51-21-8,
5-Fluorouracil 51-61-6, Dopamine, biological studies 51-98-9
52-01-7, Spironolactone 53-16-7, Estrone, biological studies
53-86-1,
Indomethacin 54-31-9, Furosemide 55-63-0, Nitroglycerin 56-12-2,
GABA, biological studies 57-41-0, Phenytoin 57-63-6
57-83-0, Progesterone, biological studies 58-00-4, Apomorphine
58-18-4, 17-Methyltestosterone 58-22-0, Testosterone 58-25-3,
Chlordiazepoxide 59-05-2, Methotrexate 59-66-5, Acetazolamide
59-92-7, L-DOPA, biological studies 60-18-4, Tyrosine, biological
studies 61-32-5, Methicillin 61-33-6, Benzylpenicillin, biological
studies 61-54-1, Tryptamine 61-72-3, Cloxacillin 66-76-2,
Dicumarol
66-79-5, Oxacillin 67-52-7D, Barbituric acid, derivs. 68-22-4
68-23-5, Norethynodrel 68-26-8, Retinol 69-53-4, Ampicillin

70-00-8, Trifluorothymidine 71-58-9, Medroxyprogesterone acetate
71-63-6, Digitoxin 72-33-3, Mestranol 76-73-3, Secobarbital
76-74-4
77-36-1, Chlorthalidone 99-66-1, Valproic acid 116-31-4, Retinal
127-47-9, Vitamin A acetate 137-58-6, Lidocaine 148-82-3, Melphalan
154-93-8, Car mustine 305-03-3, Chlorambucil 434-03-7 439-14-5,
Diazepam 512-64-1, Echinomycin 523-87-5, Dimenhydrinate 604-75-1,
Oxazepam 645-05-6, Hexamethylmelamine 745-65-3, Alprostadil
846-49-1, Lorazepam 968-81-0, Acetohexamide 1406-16-2, Vitamin D
1406-18-4, Vitamin E 2365-30-2 2898-12-6, Medazepam 3116-76-5,
Dicloxacillin 5104-49-4, Flurbiprofen 6533-00-2, Norgestrel
8064-90-2, Co-trimoxazole 12001-79-5, Vitamin K 12794-10-4D,
Benzodiazepine, derivs. 13010-47-4, Lomustine 13182-89-3,
Metronidazole benzoate 13909-02-9, PCNU 13909-09-6, Semustine
15676-16-1, Sulpiride 20830-75-5, Digoxin 22204-53-1, Naproxen
22916-47-8 23930-19-0, Alfaxalone 29767-20-2 30516-87-1
31430-15-6, Flubendazole 33125-97-2, Etomidate 33419-42-0
35121-78-9, Prostacyclin 36322-90-4, Piroxicam 41451-75-6,
Bruceantin
51264-14-3, Amsacrine 52468-60-7, Flunarizine 57998-68-2, Diaziquone
59277-89-3, Acyclovir 61422-45-5, Carmofur 65277-42-1, Ketoconazole
65886-71-7, Fazarabine 69112-98-7 77327-05-0 84625-61-6
84697-22-3 127950-65-6
(parenteral delivery systems contg. cyclodextrins or pyridine redox
systems of)

L14 ANSWER 16 OF 21 USPATFULL

AB The invention provides a method for treating sexual dysfunction in male mammals using a compound of the formula

[E--DHC]

(I)

or a non-toxic pharmaceutically acceptable salt thereof, wherein [E] is an estrogen and [DHC] is the reduced, biooxidizable, blood-brain barrier-penetrating, lipoidal form of a dihydropyridine. revreaction.pyridinium salt redox carrier. Compositions for use in the subject method are also disclosed. A preferred compound for use in the method and compositions is an estradiol derivative, namely,
17. beta.-[(1-methyl-1,4-dihydro-3-pyridinyl)carbonyloxy]estra-1,3,5(10)-trien-3-ol.

AN 89:74171 USPATFULL

TI Method for treating male sexual dysfunction

IN Anderson, Jr., Wesley R., Gainesville, FL, United States

Bodor, Nicholas S., Gainesville, FL, United States

Simpkins, James W., Gainesville, FL, United States

PA University of Florida, Gainesville, FL, United States (U.S. corporation)

PI US 4863911 19890905

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AI US 1986-892861 19860804 (6)

DT Utility

FS Granted

EXNAM Primary Examiner: Shen, Cecilia

LREP Baumeister, Mary Katherine, Clarke, Dennis P.

CLMN Number of Claims: 25

ECL Exemplary Claim: 1,14

DRWN 7 Drawing Figure(s); 7 Drawing Page(s)

LN.CNT 1370

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 4863911 19890905 <--
SUMM . . . dysfunctions, primarily because of significant undesirable
side-effects. Estrogens are, however, generally administered to control
symptoms of menopause; for postmenopausal osteoporosis,
dysmenorrhea, menorrhagia, amenorrhea, atrophic vaginitis,
ovarian dwarfism and post-partum breast engorgement; in combination
with progestins in oral contraceptives; in breast cancer; . . .
IT 50-27-1D, Estriol, dihydropyridine redox carrier conjugates 50-28-2D,
Estradiol, dihydropyridine redox carrier conjugates 50-50-0D,
Estradiol benzoate, dihydropyridine redox carrier conjugates 53-16-7D, Estrone,
dihydropyridine redox carrier conjugates 57-63-6D, Ethinyl
estradiol, dihydropyridine redox carrier conjugates 72-33-3D,
Mestranol, dihydropyridine redox carrier conjugates 152-43-2D,
Quinestrol, dihydropyridine redox carrier conjugates 313-06-4D,
Estradiol cypionate, dihydropyridine redox carrier conjugates
979-32-8D, Estradiol valerate, dihydropyridine redox carrier conjugates
3571-53-7D, Estradiol undecylate, dihydropyridine redox carrier
conjugates 3758-34-7D, dihydropyridine redox carrier conjugates
4956-37-0D, Estradiol enanthate, dihydropyridine redox carrier
conjugates 5941-36-6D, Estrazinol, dihydropyridine redox carrier conjugates
10322-73-3D, dihydropyridine redox carrier conjugates 27790-75-6D,
Dihydropyridine, derivs., estrogen conjugates 39791-20-3D, Nylestriol,
dihydropyridine redox carrier conjugates 47703-84-4D, dihydropyridine
redox carrier conjugates 117539-14-7D, estrogens conjugates
(male sexual dysfunction treatment by)

L14 ANSWER 17 OF 21 USPATFULL

AB A method, formulation, and steroid drug delivery system for the
administration of sex steroids for menstrual cycle regulation is
disclosed. The invention is useful in clinical applications for
pregnancy spacing and treatment of menstrual dysfunction. Progestin and
estrogen are administered in a treatment cycle mimicking sex steroid
hormones in the normal menstrual cycle. The steroid treatment cycle is
divided into arbitrary and discrete follicular and luteal phase
segments

beginning with the onset of menstruation. In the early segment of the
follicular phase no exogenous steroid is administered. Depending on the
clinical and/or physiologic situation of a patient, unopposed progestin
or estrogen is then administered. In the preferred embodiment an early
luteal phase follows with low dose administration of combination
estrogen/progestin; mid luteal estrogen and progestin is administered
in a dose adequate to suppress pituitary FSH and LH and to maintain the
endometrium; and terminally, a reduced dosage of combination
estrogen/progestin is administered. The clinical success of the method
and formulation depends not only upon the biologic potency of the
progestin molecule administered but also depends upon the dose and
temporal relationship of administration of exogenous estrogen,
progestin, and combination estrogen/progestin. As a consequence, any

FDA approved synthetic estrogen or progestin, in pharmacologically
appropriate dosage is suitable for formulation in accordance with the
present invention. Menstrual cycle regulation and effective
contraception is achieved by hypothalamic-pituitary dysrhythmia rather
than sustained FSH, LH, endogenous estrogen suppression. A reduced
exposure to the adverse endocrine and metabolic effects of high dose
estrogen and progestin administered concurrently is accomplished. Upon

discontinuation of the administration of the present invention, prompt FSH and subsequent LH recovery ensue, providing for an appropriate return of ovulation and appropriate menstruation in the prior to drug normal ovulating patient. The method and formulation further allow the physician to take physiologic corrective measures in menstrual dysfunction patients who may or may not seek contraception and present as hypoestrogen, euestrogen, or hyperestrogen ovulation dysfunction or anovulatory.

AN 81:53281 USPATFULL
TI Follicular phase estrogen or progestin with physiologic estrogen/progestin luteal phase replacement drug delivery system
IN Vorys, Nichols, 336 S. Columbia Ave., Columbus, OH, United States
43209
PI US 4292315 19810929 <--
AI US 1979-69275 19790824 (6)
RLI Division of Ser. No. US 1977-865851, filed on 30 Dec 1977, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Roberts, Elbert L.
LREP Kenyon & Kenyon
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 2401
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 4292315 19810929 <--
SUMM . . . replacement of the invention is useful in the management of clinical states of menstrual irregularity, menstrual dysfunction, ovulation pain, primary **dysmenorrhea**, and premenstrual tension syndrome. The method is also useful as a sex steroid drug delivery system for pregnancy spacing where. . .
SUMM . . . of menstrual irregularity, as for example, menorrhagia, hypermenorrhea, menometrorrhagia, oligomeorrhagia; 2.degree. amenorrhea (in presence of progesterone withdrawal-Prolution 100 mgm I.M.); **dysmenorrhea**, pre-menstrual tension; and for ovulation pain. For the euestrogen and hyperestrogen clinical states in which the follicular-luteal drug delivery and. . .
SUMM . . . sex steroid replacement in the management of menstrual dysfunction, i.e., hypermenorrhea, menorrhagia, primary amenorrhea, 2.degree. amenorrhea, oligomenorrhea, ovulation pains, primary **dysmenorrhea**; and a method for oral sex steroid replacement in pregnancy spacing.
IT 57-63-6 68-22-4 297-76-7
(hormonal formulations contg., for human menstrual regulation)

L14 ANSWER 18 OF 21 USPATFULL
AB Oral contraceptive consisting essentially in admixture with a pharmaceutically acceptable carrier, of 21-23 separate dosage units adapted for oral ingestion, containing an amount of an estrogen corresponding in activity to 0.030-0.050 mg.
17.alpha.-ethinylestradiol,
with the first 10-12 dosage units being in combination with a gestagen corresponding in activity to about 0.050-0.125 mg. of d-norgestrel and the remainder in combination with a gestagen corresponding in activity to 2-3 times the amount of gestagen in the first 10-12 units.
AN 76:9033 USPATFULL
TI Method for contraception by the administration of sequential contraceptive preparations
IN Lachnit-Fixson, Ursula, Berlin, Germany, Federal Republic of

PA Schering Aktiengesellschaft, Berlin & Bergkamen, Germany, Federal
 Republic of (non-U.S. corporation)
 PI US 3939264 19760217 <--
 AI US 1973-350590 19730412 (5)
 PRAI DE 1972-2218831 19720414
 DE 1973-2310963 19730303
 DT Utility
 FS Granted
 EXNAM Primary Examiner: Roberts, Elbert L.
 LREP Millen, Raptes & White
 CLMN Number of Claims: 6
 ECL Exemplary Claim: 1
 DRWN No Drawings
 LN.CNT 365
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 PI US 3939264 19760217 <--
 DETD TABLE 3

COMPARISON

Side Effects	Last Untreated		Total Number of Treatment Cycles (1,441)
	Cycle (254 Women)		
		%	%
Dysmenorrhea	7.9	1.8	
Nausea and vomiting	6.3	5.7	
Dizziness	4.7	1.3	
Other symptoms	7.5	6.7	
Tenderness of the breasts	7.9	6.8	
Headaches	13.8	8.2	
Nervousness	14.2	6.3	
Depressions.	..		
IT 51-98-9 57-63-6			
	(contraceptive sequential tablets)		

L14 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2002 ACS
 AB Seventy patients with different gynecol. disorders (dysmenorrhea, hypomenorrhea, hypermenorrhea, oligomenorrhea, irregular menses, juvenile bleeding, metrorrhage, preclimacteric irregular bleeding, secondary amenorrhea, primary and secondary sterility) were treated with Planovin, (megestrol acetate plus ethynodiol), Delpregnin (megestrol acetate plus mestranol), or niagestine (megestrol acetate). The results of this therapy in all disorders except hypomenorrhea are regarded during treatment as good to excellent; upon termination of therapy the good results decreased further. In 7 patients with amenorrhea or anovulatory cycles, the renal excretion of 17-keto steroids, corticosteroids (measured as Porter-Silber chromogen), and pregnanetriol were detd. before, during, and after treatment with Planovin. Under treatment the hormones excretion decreased significantly: on the av. of 76.6% for keto steroids, 65.0% for corticosteroids, and 56.6% for pregnanetriol, based on the level before treatment (100%). These decreases must not be considered as a diminished activity of the adrenal cortex, but are probably traceable to a reduced ovarian activity as well as the known effect of estrogen on cortisol metabolism. After

interruption of therapy the initial values were attained again quickly.
42 refs.

AN 1970:51499 CAPLUS
DN 72:51499

TI Clinical and biochemical studies on megestrol acetate and two megestrol acetate-estrogen combinations in the treatment of menstrual disorders and sterility

AU Arnold, Martin; Richter, Robert H. H.; Roth, Fritz
CS Univ.-Frauenklin., Bern, Switz.
SO Z. Geburtsh. Gynaekol. (1969), 171(2), 125-44
CODEN: ZGGNAE

DT Journal
LA German
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CODEN: ZGGNAE

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42 refs.

IT 57-63-6 72-33-3
RL: BIOL (Biological study)
(mixt. with megestrol acetate, in menstrual disorders and sterility treatment)

L14 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2002 ACS
AB Girls aged 12-18 years were treated for 10 days with Lyndiol or Anovlar
21 daily. The bleeding stopped after 4-5 days in metrorrhagia juvenilis and 4-5 days after the last dose the withdrawal bleeding occurred. The treatment normalized the bleeding in hypermenorrhea, hypooligomenorrhea, and amenorrhea secundaria. In 2 of 7 cases with hypooligomenorrhea and amenorrhea secundaria there was a sudden bleeding in the 7-8th day of the treatment. The withdrawal bleeding in **dysmenorrhea**, where treatment was continued for 21 days beginning in the 5th day of the cycle, was painless. The treatment normalized the cytological picture of the vaginal smears in all cases.

AN 1968:441530 CAPLUS
DN 69:41530

TI Treatment of menstruation disorders with gestagens
AU Komorowska, Alina
CS Akad. Med., Lodz, Poland
SO Ginekol. Pol. (1968), 39(1), 59-66

DT CODEN: GIPOA3
LA Polish
SO Ginekol. Pol. (1968), 39(1), 59-66
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treatment. The withdrawal bleeding in **dysmenorrhea**, where
treatment was continued for 21 days beginning in the 5th day of the
cycle,
was painless. The treatment normalized the cytological picture of the
vaginal smears in all cases.
IT 57-63-6
RL: BIOL (Biological study)
(mixt. with 17-hydroxy-19-nor-17.alpha.-pregn-4-en-20-yn-3-one
acetate,
in menstruation disorder treatment)

L14 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2002 ACS
AB Patients (22) with essential **dysmenorrhea** were treated with a
combination of vinylesternolone-ethynylestradiol. All patients were
previously treated with a placebo before the beginning of medication.
Urinary pregnanediol was detd. in the group during the control cycle
(placebo) and the exptl. cycle. The compds., by inhibiting ovulation,
caused regression of the painful syndrome without producing significant
side effects. The medication also markedly decreased the urinary
elimination of pregnanediol.
AN 1967:62314 CAPLUS
DN 66:62314
TI Ovariostatic treatment of **dysmenorrhea**
AU Variati, Gianvittorio
CS Univ. Milan, Milan, Italy
SO Ann. Ostet. Ginecol. (1966), 88(8), 671-9
CODEN: AOGIAI
DT Journal
LA Italian
TI Ovariostatic treatment of **dysmenorrhea**
SO Ann. Ostet. Ginecol. (1966), 88(8), 671-9
CODEN: AOGIAI
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side effects. The medication also markedly decreased the urinary
elimination of pregnanediol.
ST OVULATION INHIBITORS **DYSMENORRHEA**; INHIBITORS OVULATION
DYSMENORRHEA; **DYSMENORRHEA** OVULATION INHIBITORS;
CONTRACEPTIVES ORAL **DYSMENORRHEA**; ORAL CONTRACEPTIVES
DYSMENORRHEA
IT 57-63-6
RL: BIOL (Biological study)
(in **dysmenorrhea** treatment)
IT 13563-60-5

RL: BIOL (Biological study)
(mixt. with 19-nor-17.alpha.-pregna-1,3,5(10)-trien-20-yne-3,17-diol,
in **dysmenorrhea** treatment)

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